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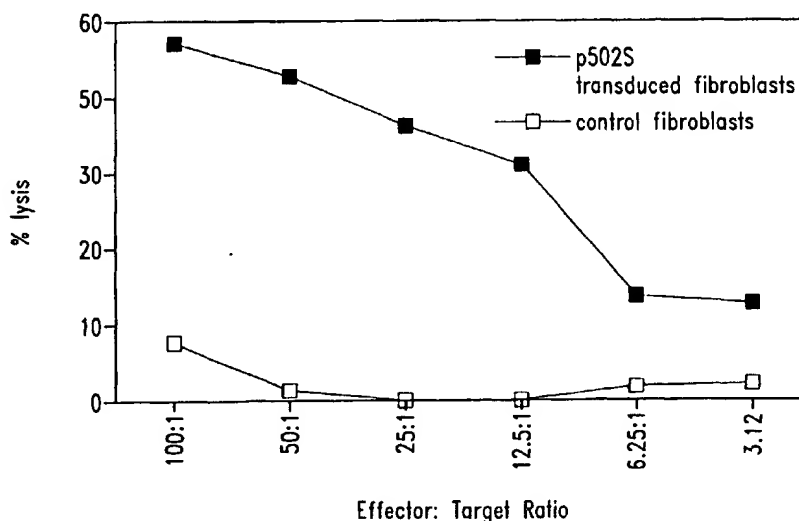
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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate-specific proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate-specific protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate-specific protein, or mRNA encoding such a protein, in a sample are also provided.

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## COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

### 5 TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate-specific protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for  
10 prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

### BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress  
15 inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but  
20 these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate  
25 with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

### 30 SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the

diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate-specific protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-550.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate-specific protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate-specific protein; and (b) a physiologically acceptable carrier. In certain embodiments, the present invention provides monoclonal antibodies that specifically bind to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 522 and 541-550, together with monoclonal antibodies comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.



Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

5        Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

10        Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

15        Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that  
20        specifically react with a prostate-specific protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described  
25        above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with one or more of:  
(i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii)  
30        an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate-specific protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

10 Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

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The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

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The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain

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embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that  
5 hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b)  
10 detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as  
15 monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed  
20 herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

#### BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The  
25 percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of  $\gamma$ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure  
30 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

5 Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse  
10 Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8<sup>+</sup> cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a <sup>51</sup>Cr release  
15 assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

20 Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

Figure 11 shows the results of an ELISA assay of antibody specificity to P501S  
25 peptides.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12

SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16

30 SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1

SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9

SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4

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SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12  
SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12  
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SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63  
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SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14  
SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14  
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SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6  
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SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860  
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861

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- SEQ ID NO: 42 is the determined cDNA sequence for P8
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SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296

SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280

SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S)

5

SEQ ID NO: 108 is the predicted amino acid sequence for F1-12

SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17

SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12 (also referred to as P501S)

SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 (also referred to as

10 P503S)

SEQ ID NO: 112 is the predicted amino acid sequence for J1-17

SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also referred to as P501S)

SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also referred to as P503S)

SEQ ID NO: 115 is the determined cDNA sequence for P89

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SEQ ID NO: 165 is the determined cDNA sequence for P195

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SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-4884  
SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-4896  
SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-4761  
30 SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-4762  
SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-4766  
SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770

- SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771
- SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-4772
- SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-4309
- SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-4278
- 5 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288
- SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283
- SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304
- SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296
- SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280
- 10 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd
- SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con
- SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev
- SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd
- SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev
- 15 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd
- SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev
- SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd
- SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev
- SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd
- 20 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev
- SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd
- SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev
- SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev
- SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd
- 25 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev
- SEQ ID NO: 223 is the determined cDNA sequence for P509S
- SEQ ID NO: 224 is the determined cDNA sequence for P510S
- SEQ ID NO: 225 is the determined cDNA sequence for P703DE5
- SEQ ID NO: 226 is the determined cDNA sequence for 9-A11
- 30 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6
- SEQ ID NO: 228 is the determined cDNA sequence for 8-H7
- SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13

- SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14  
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23  
SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24  
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25  
5 SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30  
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34  
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35  
SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36  
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38  
10 SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39  
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40  
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41  
SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42  
SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45  
15 SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46  
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51  
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56  
SEQ ID NO: 247 is the determined cDNA sequence for PTPN64  
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65  
20 SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67  
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76  
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84  
SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85  
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86  
25 SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87  
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88  
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1  
SEQ ID NO: 257 is the determined cDNA sequence for JP1F2  
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2  
30 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1  
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2  
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3

- SEQ ID NO: 262 is the determined cDNA sequence for JP1A4  
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5  
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6  
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6  
5 SEQ ID NO: 266 is the determined cDNA sequence for JP1B5  
SEQ ID NO: 267 is the determined cDNA sequence for JP1A6  
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8  
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7  
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9  
10 SEQ ID NO: 271 is the determined cDNA sequence for JP1C10  
SEQ ID NO: 272 is the determined cDNA sequence for JP1A9  
SEQ ID NO: 273 is the determined cDNA sequence for JP1F12  
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12  
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11  
15 SEQ ID NO: 276 is the determined cDNA sequence for JP1C11  
SEQ ID NO: 277 is the determined cDNA sequence for JP1C12  
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12  
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12  
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2  
20 SEQ ID NO: 281 is the determined cDNA sequence for JP8H1  
SEQ ID NO: 282 is the determined cDNA sequence for JP8H2  
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3  
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4  
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3  
25 SEQ ID NO: 286 is the determined cDNA sequence for JP8G4  
SEQ ID NO: 287 is the determined cDNA sequence for JP8B6  
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6  
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5  
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8  
30 SEQ ID NO: 291 is the determined cDNA sequence for JP8C7  
SEQ ID NO: 292 is the determined cDNA sequence for JP8D7  
SEQ ID NO: 293 is the determined cDNA sequence for P8D8

- SEQ ID NO: 294 is the determined cDNA sequence for JP8E7  
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8  
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8  
SEQ ID NO: 297 is the determined cDNA sequence for JP8B10  
5 SEQ ID NO: 298 is the determined cDNA sequence for JP8C10  
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9  
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10  
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9  
SEQ ID NO: 302 is the determined cDNA sequence for JP8H9  
10 SEQ ID NO: 303 is the determined cDNA sequence for JP8C12  
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11  
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12  
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12  
SEQ ID NO: 307 is the determined cDNA sequence for P711P  
15 SEQ ID NO: 308 is the determined cDNA sequence for P712P  
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23  
SEQ ID NO: 310 is the determined cDNA sequence for P774P  
SEQ ID NO: 311 is the determined cDNA sequence for P775P  
SEQ ID NO: 312 is the determined cDNA sequence for P715P  
20 SEQ ID NO: 313 is the determined cDNA sequence for P710P  
SEQ ID NO: 314 is the determined cDNA sequence for P767P  
SEQ ID NO: 315 is the determined cDNA sequence for P768P  
SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes  
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5  
25 SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5  
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26  
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26  
SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23  
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23  
30 SEQ ID NO: 332 is the determined full length cDNA sequence for P509S  
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9)  
SEQ ID NO: 334 is the determined cDNA sequence for P714P

- SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)
- SEQ ID NO: 336 is the predicted amino acid sequence for P705P
- SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10
- SEQ ID NO: 338 is the amino acid sequence of the peptide p5
- 5 SEQ ID NO: 339 is the predicted amino acid sequence of P509S
- SEQ ID NO: 340 is the determined cDNA sequence for P778P
- SEQ ID NO: 341 is the determined cDNA sequence for P786P
- SEQ ID NO: 342 is the determined cDNA sequence for P789P
- SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo
- 10 sapiens MM46 mRNA
- SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
- SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin
- 15 SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)
- SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)
- SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo
- 20 sapiens phosphoglucomutase-related protein (PGMRP)
- SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40
- SEQ ID NO: 350 is the determined cDNA sequence for P777P
- SEQ ID NO: 351 is the determined cDNA sequence for P779P
- 25 SEQ ID NO: 352 is the determined cDNA sequence for P790P
- SEQ ID NO: 353 is the determined cDNA sequence for P784P
- SEQ ID NO: 354 is the determined cDNA sequence for P776P
- SEQ ID NO: 355 is the determined cDNA sequence for P780P
- SEQ ID NO: 356 is the determined cDNA sequence for P544S
- 30 SEQ ID NO: 357 is the determined cDNA sequence for P745S
- SEQ ID NO: 358 is the determined cDNA sequence for P782P
- SEQ ID NO: 359 is the determined cDNA sequence for P783P

- SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984
- SEQ ID NO: 361 is the determined cDNA sequence for P787P
- SEQ ID NO: 362 is the determined cDNA sequence for P788P
- SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994
- 5 SEQ ID NO: 364 is the determined cDNA sequence for P781P
- SEQ ID NO: 365 is the determined cDNA sequence for P785P
- SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.
- SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.
- 10 SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.
- SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.
- SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 15 374.
- SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.
- SEQ ID NO: 381 is the determined cDNA sequence for B716P.
- SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.
- 20 SEQ ID NO: 383 is the predicted amino acid sequence for P711P.
- SEQ ID NO: 384 is the cDNA sequence for P1000C.
- SEQ ID NO: 385 is the cDNA sequence for CGI-82.
- SEQ ID NO: 386 is the cDNA sequence for 23320.
- SEQ ID NO: 387 is the cDNA sequence for CGI-69.
- 25 SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.
- SEQ ID NO: 389 is the cDNA sequence for 23379.
- SEQ ID NO: 390 is the cDNA sequence for 23381.
- SEQ ID NO: 391 is the cDNA sequence for KIAA0122.
- SEQ ID NO: 392 is the cDNA sequence for 23399.
- 30 SEQ ID NO: 393 is the cDNA sequence for a previously identified gene.
- SEQ ID NO: 394 is the cDNA sequence for HCLBP.
- SEQ ID NO: 395 is the cDNA sequence for transglutaminase.



SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.

SEQ ID NO:399 is the cDNA sequence for hTGR.

5 SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

SEQ ID NO:404 is the cDNA sequence for 22550.

10 SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553.

SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

15 SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.

20 SEQ ID NO:415 is the cDNA sequence for 22572.

SEQ ID NO:416 is the cDNA sequence for 22573.

SEQ ID NO:417 is the cDNA sequence for 22573.

SEQ ID NO:418 is the cDNA sequence for 22575.

SEQ ID NO:419 is the cDNA sequence for 22580.

25 SEQ ID NO:420 is the cDNA sequence for 22581.

SEQ ID NO:421 is the cDNA sequence for 22582.

SEQ ID NO:422 is the cDNA sequence for 22583.

SEQ ID NO:423 is the cDNA sequence for 22584.

SEQ ID NO:424 is the cDNA sequence for 22585.

30 SEQ ID NO:425 is the cDNA sequence for 22586.

SEQ ID NO:426 is the cDNA sequence for 22587.

SEQ ID NO:427 is the cDNA sequence for 22588.

- SEQ ID NO:428 is the cDNA sequence for 22589.  
SEQ ID NO:429 is the cDNA sequence for 22590.  
SEQ ID NO:430 is the cDNA sequence for 22591.  
SEQ ID NO:431 is the cDNA sequence for 22592.  
5 SEQ ID NO:432 is the cDNA sequence for 22593.  
SEQ ID NO:433 is the cDNA sequence for 22594.  
SEQ ID NO:434 is the cDNA sequence for 22595.  
SEQ ID NO:435 is the cDNA sequence for 22596.  
SEQ ID NO:436 is the cDNA sequence for 22847.  
10 SEQ ID NO:437 is the cDNA sequence for 22848.  
SEQ ID NO:438 is the cDNA sequence for 22849.  
SEQ ID NO:439 is the cDNA sequence for 22851.  
SEQ ID NO:440 is the cDNA sequence for 22852.  
SEQ ID NO:441 is the cDNA sequence for 22853.  
15 SEQ ID NO:442 is the cDNA sequence for 22854.  
SEQ ID NO:443 is the cDNA sequence for 22855.  
SEQ ID NO:444 is the cDNA sequence for 22856.  
SEQ ID NO:445 is the cDNA sequence for 22857.  
SEQ ID NO:446 is the cDNA sequence for 23601.  
20 SEQ ID NO:447 is the cDNA sequence for 23602.  
SEQ ID NO:448 is the cDNA sequence for 23605.  
SEQ ID NO:449 is the cDNA sequence for 23606.  
SEQ ID NO:450 is the cDNA sequence for 23612.  
SEQ ID NO:451 is the cDNA sequence for 23614.  
25 SEQ ID NO:452 is the cDNA sequence for 23618.  
SEQ ID NO:453 is the cDNA sequence for 23622.  
SEQ ID NO:454 is the cDNA sequence for folate hydrolase.  
SEQ ID NO:455 is the cDNA sequence for LIM protein.  
SEQ ID NO:456 is the cDNA sequence for a known gene.  
30 SEQ ID NO:457 is the cDNA sequence for a known gene.  
SEQ ID NO:458 is the cDNA sequence for a previously identified gene.  
SEQ ID NO:459 is the cDNA sequence for 23045.

SEQ ID NO:460 is the cDNA sequence for 23032.

SEQ ID NO:461 is the cDNA sequence for 23054.

SEQ ID NO:462-467 are cDNA sequences for known genes.

SEQ ID NO:468-471 are cDNA sequences for P710P.

5 SEQ ID NO:472 is a cDNA sequence for P1001C.

SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).

SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).

10 SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).

SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).

SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO:  
15 474.

SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.

20 SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO:  
25 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

30 SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

- SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.
- SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.
- SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.
- SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.
- SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.
- SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.
- SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.
- SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.
- SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P. SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.
- SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.
- SEQ ID NO: 526 is the full-length cDNA sequence for P790P.
- SEQ ID NO: 527 is the predicted amino acid sequence for P790P.
- SEQ ID NO: 528 & 529 are PCR primers.
- SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.
- SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.
- SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.
- SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.
- SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.
- SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.
- SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.
- SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.
- SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.
- SEQ ID NO: 539 is the peptide P501S-370.
- SEQ ID NO: 540 is the peptide P501S-376.
- SEQ ID NO: 541-550 are epitopes of P501S.
- SEQ ID NO: 551 corresponds to amino acids 543-553 of P501S.

## DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate-specific polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate-specific protein or a variant thereof. A "prostate-specific protein" is a protein that is expressed in normal prostate and/or prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a non-prostate normal tissue, as determined using a representative assay provided herein. Certain prostate-specific proteins are proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate-specific proteins. Sequences of polynucleotides encoding certain prostate-specific proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Sequences of polypeptides comprising at least a portion of a prostate-specific protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

## PROSTATE-SPECIFIC PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate-specific protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred

polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate-specific protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate-specific protein. Polynucleotides complementary to any such sequences are also  
5 encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the  
10 present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate-specific protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions  
15 and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate-specific protein or a portion thereof. The  
20 term "variants" also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local  
25 regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the  
30 Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices

for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenesis pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate-specific protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such

as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example,  
5 a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate-specific than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997).  
10 Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate-specific cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

15 An amplified portion may be used to isolate a full length gene from a suitable library (*e.g.*, a prostate-specific cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes.  
20 Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with  $^{32}\text{P}$ ) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A*  
25 *Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The  
30 complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into



a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments; using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate-specific protein are provided in SEQ ID NO:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536.

Isolation of these polynucleotides is described below. Each of these prostate-specific proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a prostate-specific protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (*e.g.*, by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate-specific polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In Huber and Carr, Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (*e.g.*, promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3'

ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

5 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector  
10 will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for  
15 therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (*e.g.*, avian pox virus). The polynucleotides may also be administered as naked plasmid vectors.  
20 Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary  
25 skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane  
30 vesicle). The preparation and use of such systems is well known in the art.

## PROSTATE-SPECIFIC POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate-specific protein or a variant thereof, as described herein. As noted above, a "prostate-specific protein" is a protein that is expressed by normal prostate and/or prostate tumor cells. Proteins that are prostate-specific proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate-specific protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate-specific protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the

immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example,  $^{125}\text{I}$ -labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate-specific protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate-specific protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino

acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known prostate-specific protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner),

preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are

located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present  
5 invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO  
10 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The  
15 lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as  
20 LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been  
25 exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion  
30 incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its



original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector  
5 that is not a part of the natural environment.

#### BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate-specific protein. As used herein, an  
10 antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate-specific protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate-specific protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding  
15 constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about  $10^3$  L/mol. The binding constant may be determined using methods well known in the art.

20 Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate-specific protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals  
25 without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the  
30 above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Most preferably, antibodies employed in the inventive methods have the ability to induce lysis of tumor cells by activation of complement and mediation of antibody-dependent cellular cytotoxicity (ADCC). Antibodies of different classes and subclasses differ in these properties. For example, mouse antibodies of the IgG2a and IgG3 classes are capable of activating serum complement upon binding to target cells which express the antigen against which the antibodies were raised, and can mediate ADCC.

Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells

and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are  
5 selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse.  
10 Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

The preparation of mouse and rabbit monoclonal antibodies that specifically bind to  
15 polypeptides of the present invention is described in detail below. However, the antibodies of the present invention are not limited to those derived from mice. Human antibodies may also be employed in the inventive methods and may prove to be preferable. Such antibodies can be obtained using human hybridomas as described by Cote *et al.* (Monoclonal Antibodies and Cancer Therapy, Alan R. Lisa, p. 77, 1985). The present invention also encompasses antibodies made by  
20 recombinant means such as chimeric antibodies, wherein the variable region and constant region are derived from different species, and CDR-grafted antibodies, wherein the complementarity determining region is derived from a different species, as described in US Patents 4,816,567 and 5,225,539. Chimeric antibodies may be prepared by splicing genes for a mouse antibody molecule having a desired antigen specificity together with genes for a human antibody molecule having the  
25 desired biological activity, such as activation of human complement and mediation of ADCC (Morrison *et al. Proc. Natl. Acad. Sci. USA* 81:6851, 1984; Neuberger *et al. Nature* 312:604, 1984; Takeda *et al. Nature* 314:452, 1985).

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard  
30 techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*,

Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to

Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

5           It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or  
10   linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

          A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent  
15   No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating  
20   compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

          A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of  
25   a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

#### T CELLS

30           Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate-specific protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral

blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from Nexell Therapeutics Inc., Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated  
5 humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate-specific polypeptide, polynucleotide encoding a prostate-specific polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate-specific  
10 polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate-specific polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a  
15 variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell  
20 proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate-specific polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of  
25 the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a prostate-specific polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Prostate-specific protein-specific T cells may be expanded using  
30 standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a prostate-specific polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate-specific polypeptide, or a short peptide  
5 corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate-specific polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate-specific protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

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#### PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds  
15 and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally  
20 described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the  
25 composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression  
30 systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression

in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (*e.g.*, polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA



or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- $\gamma$ , TNF $\alpha$ , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10 ) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example,

an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent  
5 adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release  
10 formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix  
15 and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical  
20 compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the  
25 antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or  
30 progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy,

*Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take-up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface  
5 receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone  
10 marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into  
15 dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this  
20 nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc $\gamma$  receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II  
25 MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a prostate-specific protein (or portion or other variant thereof) such that the prostate-specific polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex*  
30 *vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection

that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells  
5 with the prostate-specific polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of  
10 the polypeptide.

#### CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical  
15 compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor.  
20 Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react  
25 against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not  
30 necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer

cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate  
5 antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in*  
10 *vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte,  
15 fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies  
20 have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back  
25 into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established  
30 using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered

over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50%  
5 above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-  
10 vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25  $\mu$ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active  
15 compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate-specific protein generally correlate with an improved clinical outcome. Such immune responses may generally be  
20 evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or  
25 more prostate-specific proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the  
30 agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer.

In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g., Harlow and Lane, 5 Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized  
10 on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G,  
15 protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full  
20 length prostate-specific proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or  
25 disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization"  
30 refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a

membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of  
5 binding agent ranging from about 10 ng to about 10  $\mu$ g, and preferably about 100 ng to about 1  $\mu$ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the  
10 binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may  
15 be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The  
20 amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween  
25 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer.  
30 Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by



assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains  
5 a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of  
10 time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group  
15 (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a  
20 signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is  
25 determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest  
30 to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along

the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1  $\mu$ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate-specific polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate-specific protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate-specific protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a prostate-specific polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that

expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may  
5 be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with prostate-specific polypeptide (*e.g.*, 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate-specific polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8<sup>+</sup> T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater  
10 and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate-specific protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to  
15 amplify a portion of a prostate-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate-specific protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate-specific protein may be used in a hybridization  
20 assay to detect the presence of polynucleotide encoding the protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate-specific protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in  
25 length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15  
30 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Techniques for both PCR based assays and hybridization assays

are well known in the art (*see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989*).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate-specific protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for proteins provided herein may be combined with assays for other known tumor antigens.

## DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For  
5 example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate-specific protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or  
10 indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate-specific protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate-specific protein. Such an oligonucleotide may be used, for example, within a PCR or  
15 hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate-specific protein.

The following Examples are offered by way of illustration and not by way of limitation.

## EXAMPLES

### EXAMPLE 1

#### 5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate  
10 tumor poly A<sup>+</sup> RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning  
kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol.  
Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and  
total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the  
manufacturer. The poly A<sup>+</sup> RNA was then purified using a Qiagen oligotex spin column mRNA  
15 purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-  
strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was  
synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with  
NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the  
cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into  
20 ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was  
prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by  
determining the number of independent colonies, the percentage of clones that carried insert, the  
average insert size and by sequence analysis. The prostate tumor library contained  $1.64 \times 10^7$   
25 independent colonies, with 70% of clones having an insert and the average insert size being 1745  
base pairs. The normal pancreas cDNA library contained  $3.3 \times 10^6$  independent colonies, with 69%  
of clones having inserts and the average insert size being 1120 base pairs. For both libraries,  
sequence analysis showed that the majority of clones had a full length cDNA sequence and were  
synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

30 cDNA library subtraction was performed using the above prostate tumor and normal  
pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some  
modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as

follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of H<sub>2</sub>O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As  
5 recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H<sub>2</sub>O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with  
10 BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H<sub>2</sub>O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and  
15 incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H<sub>2</sub>O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA  
20 was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK<sup>+</sup> (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and  
25 grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively,  
30 with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor  
5 expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid  
10 sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and  
15 mitochondria cytochrome C oxidase subunit II. Specifically, 1  $\mu$ g each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

20 Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21,  
25 K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified  
30 human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA



library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show  
5 some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid  
10 sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided  
15 in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein,  
20 mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in  
30 SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated

clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA<sup>+</sup> RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni,

Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively.

## EXAMPLE 2

### DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2  $\mu$ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR,  $\beta$ -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using  $\beta$ -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the  $\beta$ -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the  $\beta$ -actin levels were determined for each

reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney,

but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

20

### EXAMPLE 3

#### ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences  
5 for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the  
10 isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-  
15 170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA  
20 sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary  
25 (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a  
30 portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of

2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.



An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity  
5 to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA  
10 sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of  
15 P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX\_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. The putative full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 525.

20 Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and  
25 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal  
30 prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the  
5 cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence  
10 being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no  
15 significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

20 Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an ORF which encodes the amino acid sequence of SEQ ID NO: 479.  
25 The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483.

Subsequent studies led to the identification of a genomic region on chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the  
30 genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led

to the identification of a potential open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

#### EXAMPLE 4

##### SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

#### EXAMPLE 5

##### FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the

subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most

recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350, 351 and 353-365.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

## EXAMPLE 6

## PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

5 6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID  
10 NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100 $\mu$ g of P2S#12 and 120 $\mu$ g of an I-A<sup>b</sup> binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6 x 10<sup>6</sup> cells/ml in complete media (RPMI-1640; Gibco  
15 BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2 x 10<sup>-5</sup> M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml  $\beta$ 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7 $\mu$ g/ml dextran sulfate and 25 $\mu$ g/ml LPS for 3 days). Six days later, cells (5 x  
20 10<sup>5</sup>/ml) were restimulated with 2.5 x 10<sup>6</sup>/ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and 3 x 10<sup>6</sup>/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb  
25 tumor cells (1 x 10<sup>4</sup> cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( 5 x 10<sup>5</sup> cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in  
30 Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2Kb were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-A<sup>b</sup> binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells ( $5 \times 10^5$ /ml) were restimulated with  $2.5 \times 10^6$ /ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

#### EXAMPLE 7

##### 10 PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100  $\mu$ g P501S in the vector VR1012 either intramuscularly or intradermally. 15 The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at 20 least one naturally processed HLA-A2-restricted CTL epitope.

#### EXAMPLE 8

##### 25 ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8<sup>+</sup> T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van 30 Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8<sup>+</sup> T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a  $\gamma$ -interferon



ELISPOT assay (see Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on  $10^4$  fibroblasts in the presence of 3  $\mu\text{g/ml}$  human  $\beta_2$ -microglobulin and 1  $\mu\text{g/ml}$  P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the fibroblasts were treated with 10 ng/ml  $\gamma$ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a  $\gamma$ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

## EXAMPLE 9

### ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GMCSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation,  $\text{CD8}^+$  cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts retrovirally transduced

to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays ( $^{51}\text{Cr}$  release) and interferon-gamma production (Interferon-gamma Elispot; *see above and Lalvani et al., J. Exp. Med. 186:859-865, 1997*). The results of these assays are presented in Figures 6A and 6B.

#### EXAMPLE 10

##### IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A PROSTATE-SPECIFIC ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100  $\mu\text{g}$  of p5 peptide together with 140  $\mu\text{g}$  of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived

from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 ug/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures, CTL recognition of p5-pulsed target cells was demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

#### EXAMPLE 11

##### 10                    EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN    IN PROSTATE

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is provided in SEQ ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly expressed in breast tumor, prostate tumor, normal prostate and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach).

#### EXAMPLE 12

##### 30                    GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND    STIMULATION TECHNIQUES WITH PROSTATE-SPECIFIC ANTIGEN

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- $\gamma$  ELISPOT analysis as described above. Using a panel of  
5 HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a  
10 multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3  $\mu$ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that  
15 specifically produced interferon- $\gamma$  when stimulated with P501S and CD80-transduced autologous fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- $\gamma$  in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

20 To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN- $\gamma$  ELISPOT assays against these A2Kb targets transduced with the "library" of P501S  
25 fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were  
30 also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN- $\gamma$  assay. Only peptides

P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

5 In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8+ T cells were cultured with autologous CD40  
10 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as  
15 demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-  
20 P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

### EXAMPLE 13

#### IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

25

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in  
30 prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences

SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

5

Table I  
Summary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97%

of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

10

## EXAMPLE 14

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS  
BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which



expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II

Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups:

10 Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group

15 libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III  
Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV  
Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57
439	22851	PAP

440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

## EXAMPLE 15

FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY  
ANALYSIS

5

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened  
10 using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-461 represent novel genes. The others (SEQ ID NO: 454-458 and 461-467) correspond to known sequences.

15

## EXAMPLE 16

## FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

20

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane

filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four  
5 sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene.

### EXAMPLE 17

#### PROTEIN EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

10

This example describes the expression and purification of the prostate-specific antigen P501S in *E. coli*, baculovirus and mammalian cells.

##### a) Expression in *E. coli*

15

Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an  
20 antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min,  
25 and lastly by 1 cycle of 72°C for 10 min. The PCR product was cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The resulting culture was  
30 induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A

(Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

5 An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR  
10 product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as Ra12-P501S-N) was confirmed by DNA sequencing.

The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands  
15 were also observed, probably due to aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen  
20 Ra12 (SEQ ID NO: 484) was prepared as follows. P501S DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

25 The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C fusion was used for expression in BL21CodonPlus induced by CE6 phage.

b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBac1. The recombinant bacmid and baculovirus were prepared according to the manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD\_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

c) Expression of P501S in mammalian cells

Full-length P501S (553AA) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The Fugene/DNA mixture

was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15  $\mu$ l of GenePorter was diluted in 500  $\mu$ l of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2  $\mu$ g of plasmid DNA that was diluted in 500  $\mu$ l of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

#### EXAMPLE 18

##### PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

###### 20 a) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to



generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

Table V

Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant ( $\mu\text{g/ml}$ )
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1  $\mu\text{g/ml}$ , followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate

specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr.

HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L) Affinipure F(ab') fragment (Jackson ImmunoResearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors, 5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

#### b) Preparation and Characterization of Antibodies against P503S

A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits

and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

5

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows.

The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further

15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception  
5 of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

10 Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat  
15 anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal,  
20 breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary,  
25 pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal  
30 antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the

appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

5 **c) Preparation and Characterization of Antibodies against P703P**

Rabbits were immunized with either a truncated (P703Ptrl; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptrl attached to a solid support. Rabbit monoclonal  
10 antibodies were isolated using SLAM technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptrl	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptrl	Rabbit monoclonal
8H2	P703Ptrl	Rabbit monoclonal
7H8	P703Ptrl	Rabbit monoclonal

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal  
20 antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

25 The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk-/- cells either untransfected or transfected with a plasmid

expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

#### EXAMPLE 19

##### CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains. Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as

described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of  
5 SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparagine, was synthesized as described above. A Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the  
10 following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether. The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was  
15 determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence  
20 using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and stained as  
25 above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (i.e. intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

30 To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM



sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C. Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by  
5 SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma  
10 membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter  
15 plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with  
20 phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates  
25 were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

30 In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above.

To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as  
5 described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were  
10 recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

The chromosomal location of P501S was determined using the GeneBridge 4  
15 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server (<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the  
20 probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al. Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

25 From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

30

## CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536;

(b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and

(c) complements of any of the sequence of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID No: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

4. An isolated polynucleotide encoding at least 15 contiguous amino acid residues of a prostate-specific protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the protein  
5 comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413,  
10 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a prostate-specific protein, or a  
15 variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396,  
20 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide comprising a sequence recited in any one  
25 of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530,  
30 531, 533, 535 and 536.

7. An isolated polynucleotide comprising a sequence that hybridizes under moderately stringent conditions to a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536.
8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.
9. An expression vector comprising a polynucleotide according to any one of claims 4-8.
10. A host cell transformed or transfected with an expression vector according to claim 9.
11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate-specific protein, the protein comprising an amino acid sequence encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536 or a complement of any of the foregoing polynucleotide sequences.

12. A monoclonal antibody that specifically binds to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 519, 520, 522 and 539-551.
- 5 13. A monoclonal antibody comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.
- 10 14. A fusion protein comprising at least one polypeptide according to claim 1.
- 15 15. A fusion protein according to claim 14, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.
- 16 16. A fusion protein according to claim 14, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.
- 17 17. A fusion protein according to claim 14, wherein the fusion protein comprises an affinity tag.
- 18 18. An isolated polynucleotide encoding a fusion protein according to claim 14.
- 25 19.. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:
- (a) a polypeptide according to claim 1;
  - (b) a polynucleotide according to claim 4;
  - (c) an antibody according to any one of claims 11-13;
  - 30 (d) a fusion protein according to claim 14; and

(e) a polynucleotide according to claim 18.

20. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- 5 (a) a polypeptide according to claim 1;  
(b) a polynucleotide according to claim 4;  
(c) an antibody according to any one of claims 11-13;  
(d) a fusion protein according to claim 14; and  
(e) a polynucleotide according to claim 18.

10

21. A vaccine according to claim 20, wherein the immunostimulant is an adjuvant.

22. A vaccine according to claim 20, wherein the immunostimulant  
15 induces a predominantly Type I response.

23. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 19.

20

24. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.

25. A pharmaceutical composition comprising an antigen-presenting cell  
25 that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

26. A pharmaceutical composition according to claim 25, wherein the antigen presenting cell is a dendritic cell or a macrophage.

27. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with an immunostimulant.
- 5 28. A vaccine according to claim 27, wherein the immunostimulant is an adjuvant.
29. A vaccine according to claim 27, wherein the immunostimulant induces a predominantly Type I response.
- 10 30. A vaccine according to claim 27, wherein the antigen-presenting cell is a dendritic cell.
31. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, and thereby inhibiting the development of a cancer in the patient.
- 20 32. A method according to claim 31, wherein the antigen-presenting cell is a dendritic cell.
33. A method according to any one of claims 23, 24 and 31, wherein the cancer is prostate cancer.
- 25 34. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- 30



(i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

5            wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate-specific protein from the sample.

35.        A method according to claim 34, wherein the biological sample is  
10        blood or a fraction thereof.

36.        A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.

15

37.        A method for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with at least one component selected from the group consisting of:

- (i)        a polypeptide according to claim 1;
- 20        (ii)        a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;
- (iii)        a polynucleotide encoding a polypeptide of (i) or (ii); and
- (iv)        an antigen presenting cell that expresses a polypeptide of (i) or (ii),
- 25        under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

38.        An isolated T cell population, comprising T cells prepared according to the method of claim 37.

30

39. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 38.

5 40. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

- (i) a polypeptide according to claim 1;
- 10 (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;
- (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
- 15 (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

20

41. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

- 25 (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;
- 30 (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

5 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

42. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

10 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111,  
15 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

20 (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

43. A method according to claim 42, wherein the binding agent is an antibody.

25

44. A method according to claim 43, wherein the antibody is a monoclonal antibody.

45. A method according to claim 42, wherein the cancer is prostate  
30 cancer.

46. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient at a first point  
5 in time with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;
- 10 (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the  
15 amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

47. A method according to claim 46, wherein the binding agent is an antibody.

20

48. A method according to claim 47, wherein the antibody is a monoclonal antibody.

49. A method according to claim 46, wherein the cancer is a prostate  
25 cancer.

50. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient with an  
30 oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein,

wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

5           (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

          (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

10

51. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

15           52. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

53. A method for monitoring the progression of a cancer in a patient,  
20 comprising the steps of:

          (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315,  
25 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

          (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

          (c) repeating steps (a) and (b) using a biological sample obtained from  
30 the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

5           54. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

10           55. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

          56. A diagnostic kit, comprising:  
          (a) one or more antibodies according to claim 11; and  
15           (b) a detection reagent comprising a reporter group.

          57. A kit according to claim 56, wherein the antibodies are immobilized on a solid support.

20           58. A kit according to claim 56, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

          59. A kit according to claim 56, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups,  
25 enzymes, biotin and dye particles.

          60. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is  
30 encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45,

47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 5 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides.

61. A oligonucleotide according to claim 60, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO:  
10 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536.

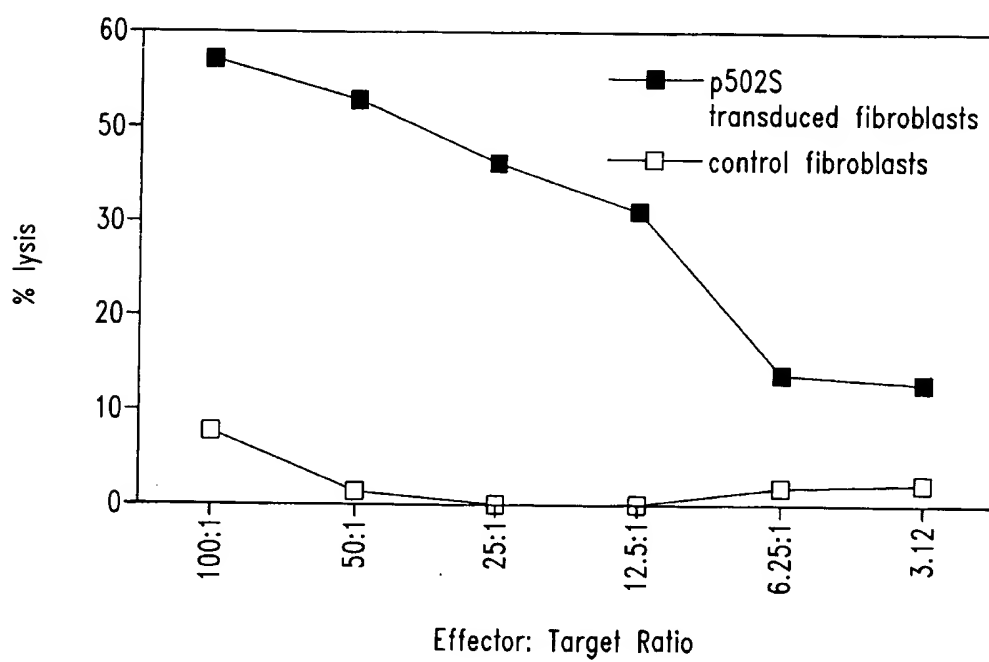
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62. A diagnostic kit, comprising:  
(a) an oligonucleotide according to claim 61; and  
(b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

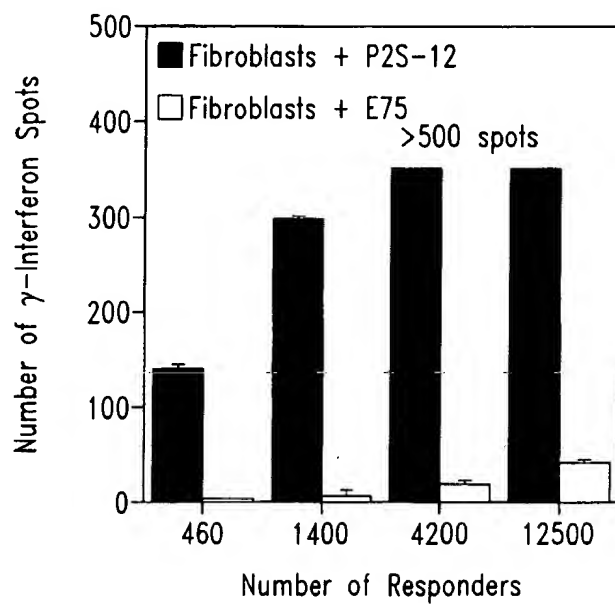
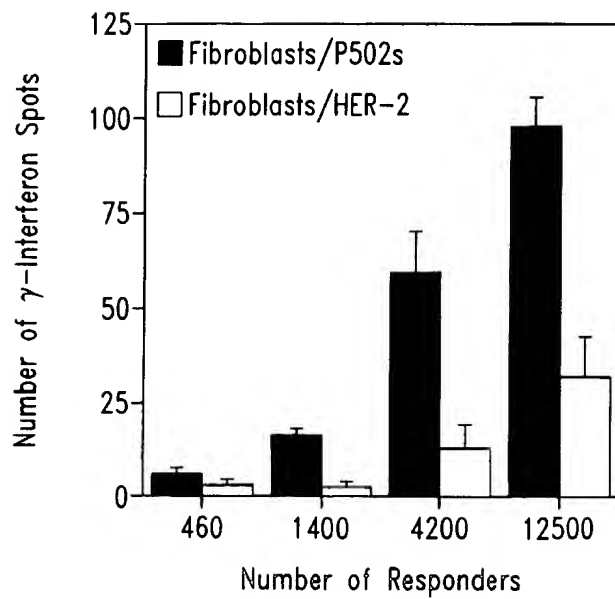
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63. A host cell according to claim 10, wherein the cell is selected from the group consisting of: *E. coli*, baculovirus and mammalian cells.

64. A recombinant protein produced by a host cell according to claim  
25 10.

*Fig. 1*



*Fig. 2A**Fig. 2B*

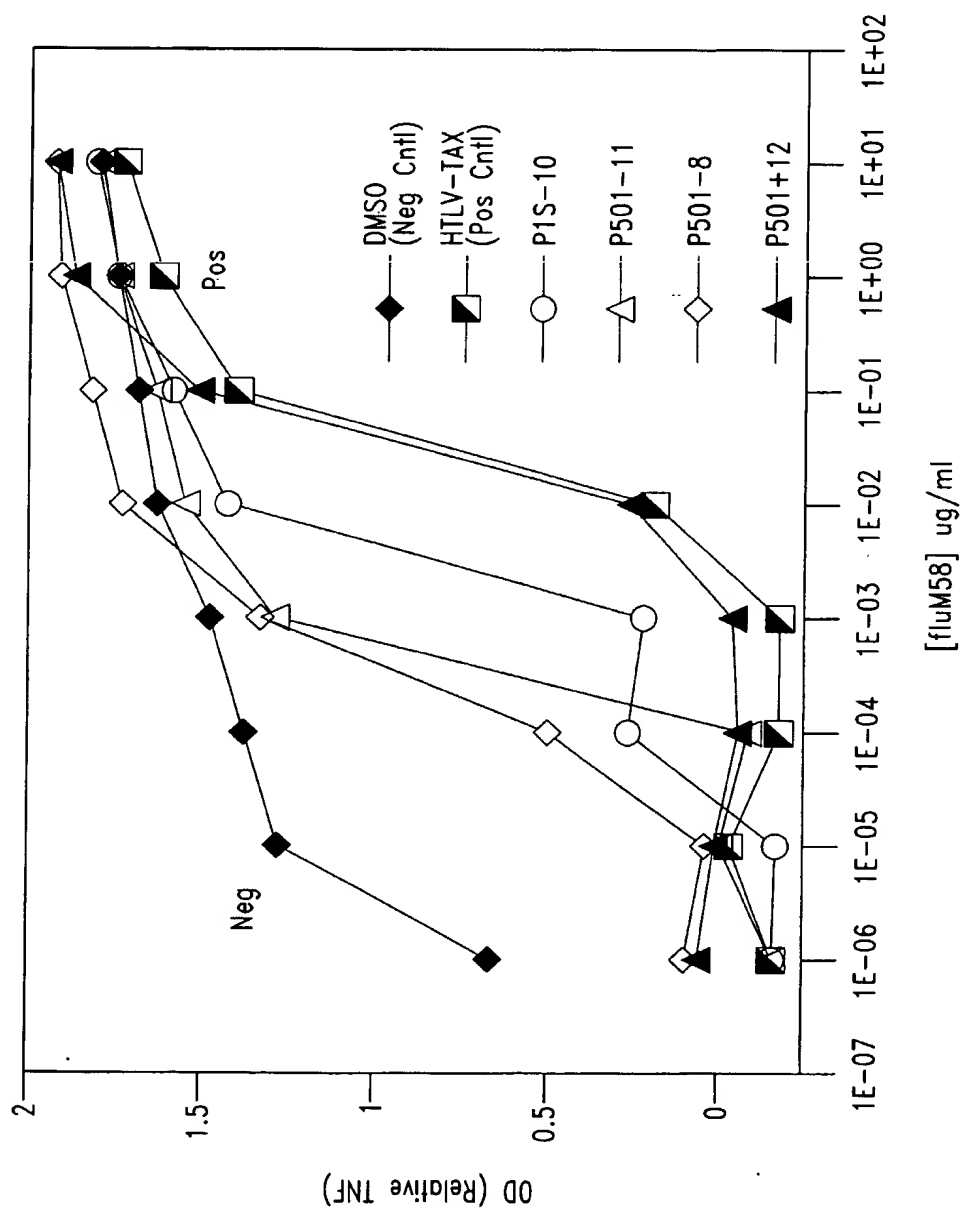
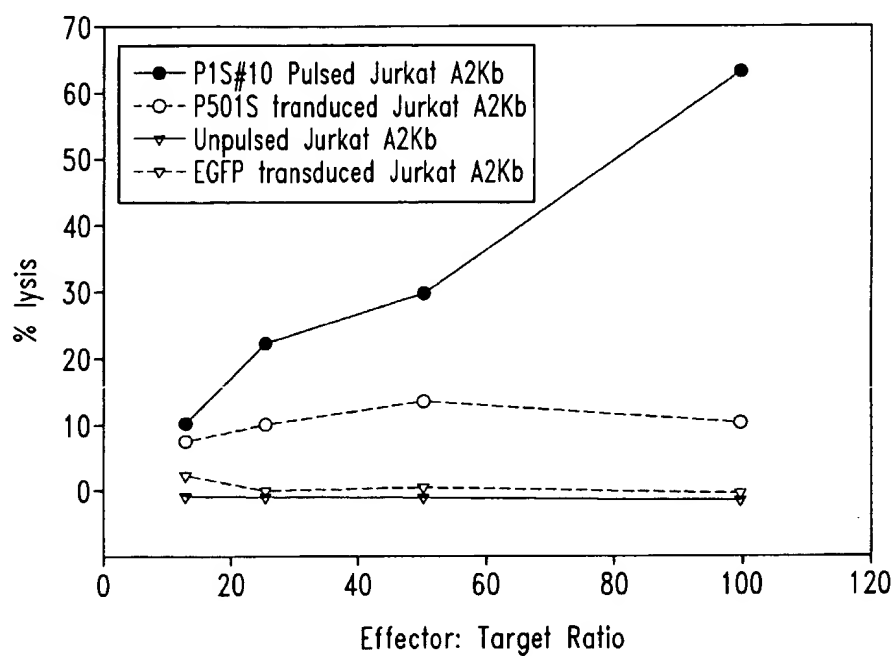
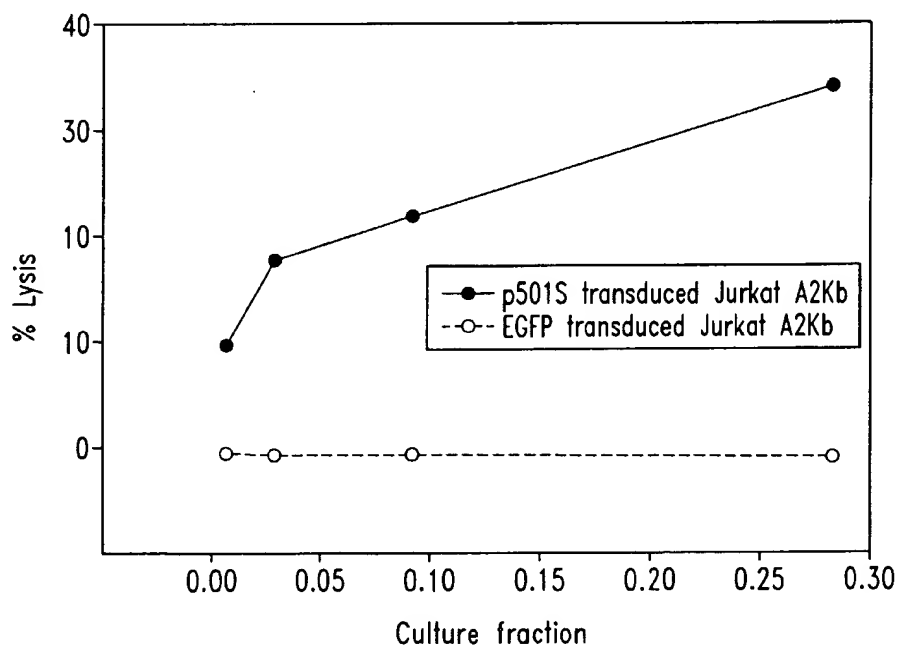
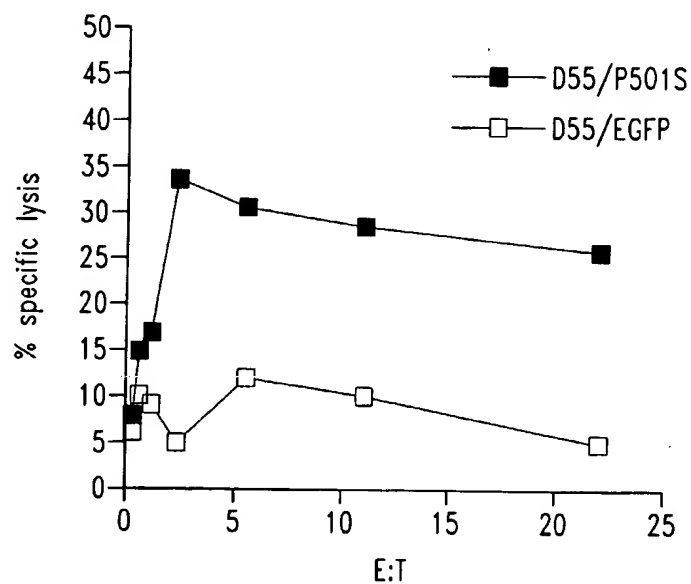
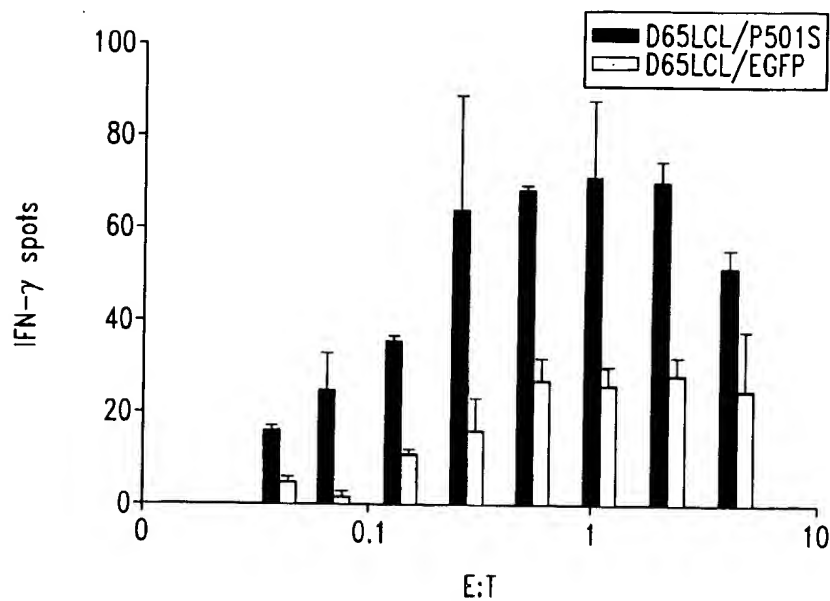
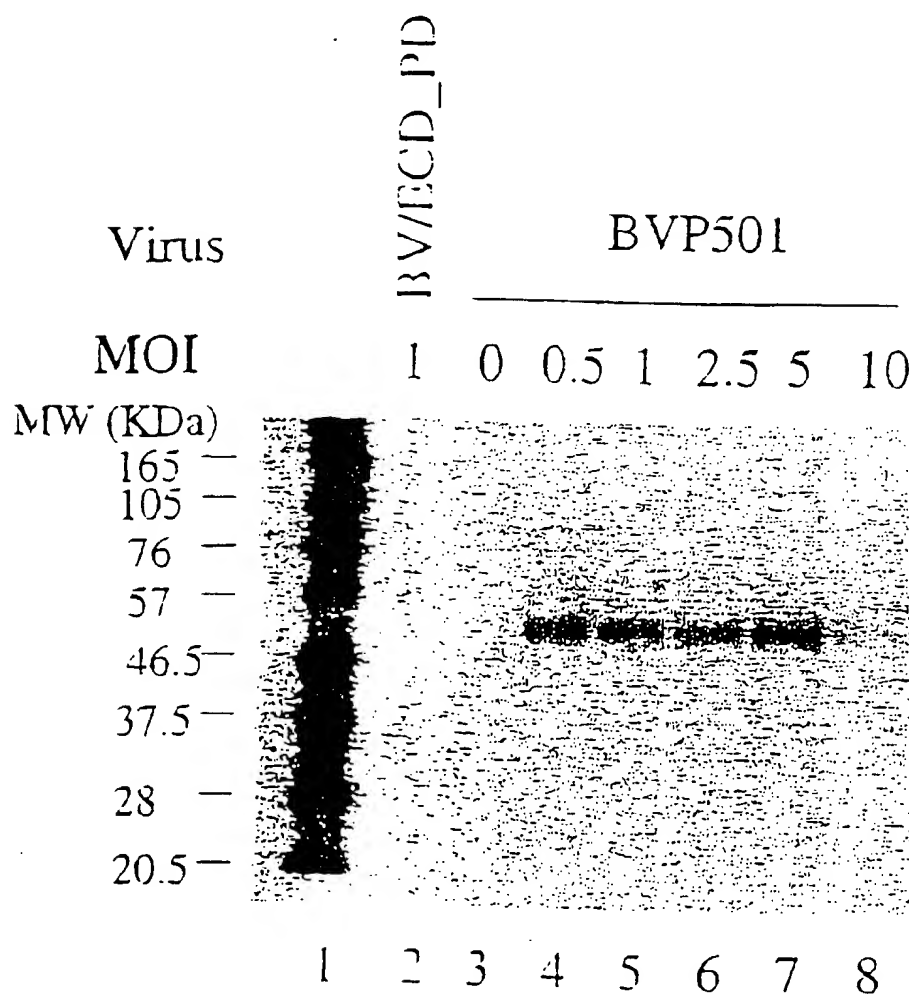


Fig. 3

*Fig. 4**Fig. 5*

*Fig. 6A**Fig. 6B*

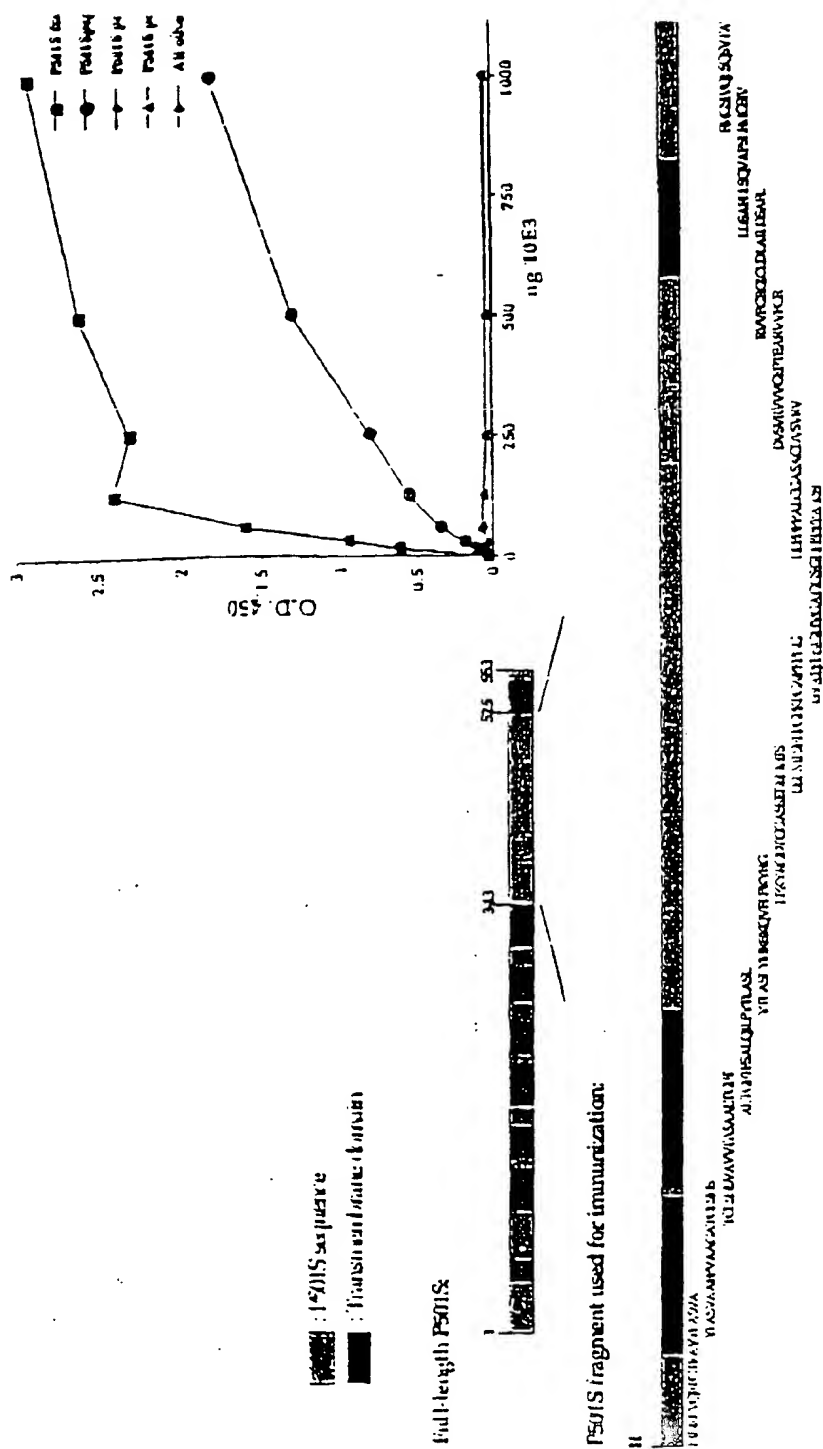
# Expression of P501S by the Baculovirus Expression System



0.6 million high 5 cells in 6-well plate were infected with an unrelated control virus BV/ECD\_PD (lane 2), without virus (lane 3), or with recombinant baculovirus for P501 at different MOIs (lane 4 - 8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

Fig. 7

**Figure 8. Mapping of the epitope recognized by 10E3-G4-D3**



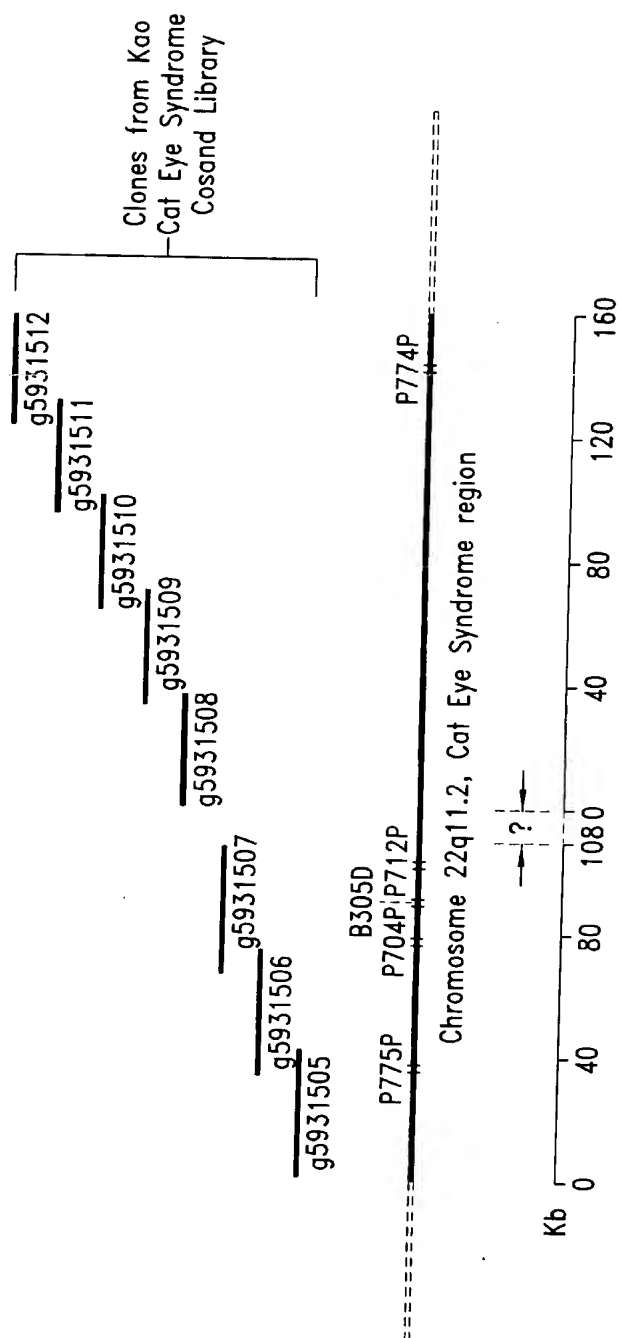
Schematic of P501S with predicted  
transmembrane, cytoplasmic, and extracellular regions

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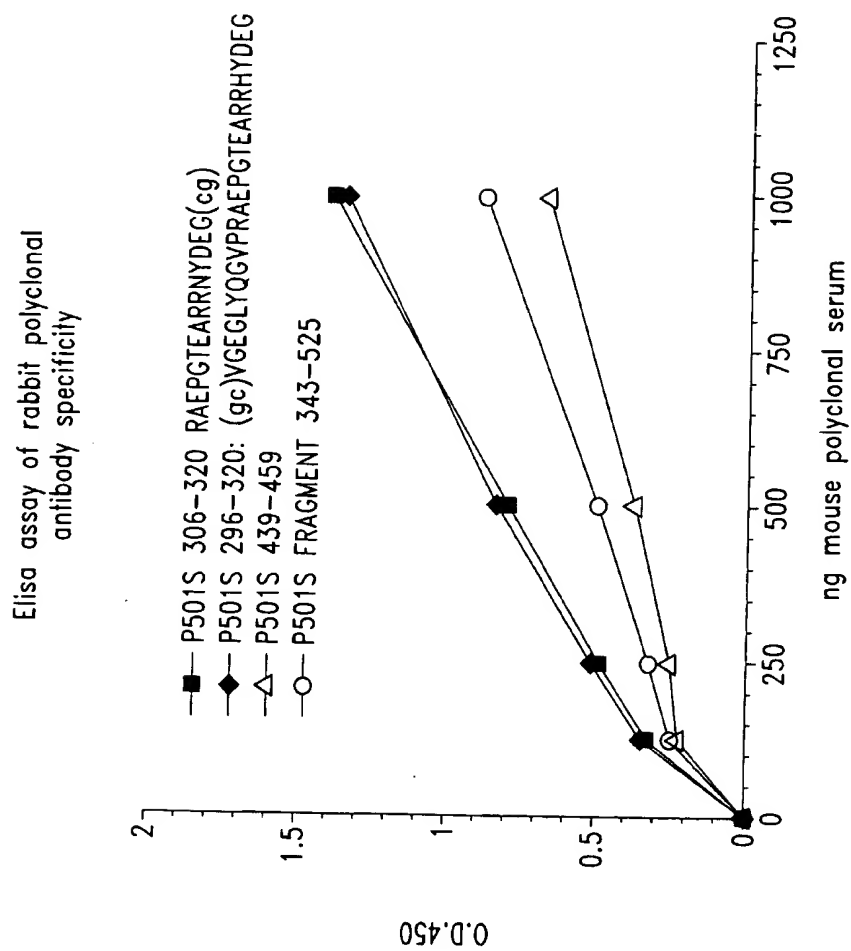
Underlined sequence: Predicted transmembrane domain; **Bold sequence:**  
 Predicted extracellular domain; *Italic sequence:* Predicted intracellular  
 domain. Sequence in bold/underlined: used generate polyclonal rabbit  
 serum

Localization of domains predicted using HMMTOP (G.E. Tusnady and I. Simon  
 (1998) Principles Governing Amino Acid Composition of Integral Membrane  
 Proteins: Applications to topology Prediction. J. Mol Biol. 283, 489-506.

*Fig. 9*

*Fig. 10*



*Fig. 11*

## SEQUENCE LISTING

<110> Corixa Corporation  
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Skeiky, Yasir A.W.  
Wang, Aijun

<120> COMPOSITIONS AND METHODS FOR THE THERAPY AND  
DIAGNOSIS OF PROSTATE CANCER

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&lt;210&gt; 6

&lt;211&gt; 818

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(818)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 6

tttttttttt	tttttttttt	aagaccctca	tcaatagatg	gagacatata	gaaatagtca	60
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ttantangg	ctantatgaa	gaacttttgg	antggaaatta	aatcaatngc	ttggccggaa	720
gtcattanga	nggctnaaaa	ggccctgtta	nggggtctgg	ctnggtttta	cccnacccat	780
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&lt;210&gt; 7

&lt;211&gt; 817

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(817)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 7

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gaagtatgta	ggaattgaag	attaatccgc	cgtagtcggt	gttctcctag	gttcaatacc	420
attgggtggc	aattgatttg	atggtaaggg	gagggatcgt	tgaactcgtc	tgttatgtaa	480
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gaatnttnng	gaaaagggct	tacaggacta	gaaaccaaata	angaaaanta	atnntaangg	660
cnttatcntn	aaaggtgnata	accnctccta	tnatcccacc	caatngnatt	ccccacncnn	720
acnattggat	nceccanttc	canaaaanggc	cnccccccgg	tgnannccnc	cttttgttcc	780
cttnantgan	ggttattcnc	ccctngcntt	atcance			817

&lt;210&gt; 8

&lt;211&gt; 799

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(799)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 8

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ctccttacia	ccacannatg	cccggctcct	cccggaaacc	antcccancc	tgngaaggat	540
caagncctgn	atccactnnt	netanaaccg	gcncncncg	cngtggaaac	cnccttntgt	600
tccttttctt	tnagggttaa	tnnecgcttg	gccttnccan	ngtcctncnc	nttttccnnt	660

gttnaaattg ttangcnecc necntecen ennnnnnan cccgaccnn annttnnann 720  
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 ctttccctct nggganncg 799

<210> 9  
 <211> 801  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(801)  
 <223> n = A,T,C or G

<400> 9  
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 caaggacaag gccaccaggt gcgggggccc aagcccatat gatccttact ctatgagcaa 180  
 aatccctctg gggggtctct ccttgaagtc cgccancagg gctcagtctt tggacccang 240  
 caggtcatgg ggttgtngnc caactggggg ccncaacgca aaanggenca gggcctcngn 300  
 caccateccc angacgcggc tacactnctg gacctccnc tccaccactt tcatgcgctg 360  
 ttentacccg cgnatntgtc ccantgttt cngtgccnac tccancttct nggacgtgcg 420  
 ctacatacgc ccggantcnc nctcccgctt tgtccctatc cacgtncan caacaaattt 480  
 cncntantg caccnatcc cacntttnc agntttcnc nncgngcttc cttntaaaag 540  
 ggttgancec cggaaaatnc cccaaagggg gggggccngg tacccaactn cccctnata 600  
 gctgaantcc ccatnacenn gnctcnatgg anccntcent tttaannacn ttctnaactt 660  
 gggaanance ctcgncntn ccccnttaa tcccncttg cnangnnent ccccnntec 720  
 nccnnntng gcntntnann cnaaaaaggc cennnancaa tctcctnncn cctcanttcg 780  
 ccancectcg aaatcgccn c 801

<210> 10  
 <211> 789  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(789)  
 <223> n = A,T,C or G

<400> 10  
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 aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttccctgc 240  
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 ccattcctga tagtgettcc tgetgtccca ngtggcccca tccctgttta tgggtccat 480  
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 gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncanct nggggggtng 780  
 gnggttccc 789

<210> 11  
 <211> 772

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(772)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 11

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ccccacctac ccaaataatta gacaccaaca cagaaaagct agcaatggat tcccttctac      60
tttgtaaataa aaataagtta aatattttaa tgcctgtgtc tctgtgatgg caacagaagg      120
accaacaggc cacatcctga taaaaggtaa gaggggggtg gatcagcaa aagacagtgc      180
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tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggaggcta gctgttaacc      420
ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc      480
ctccctgtat aagtcacagac tgaaaccccc ttggaaggnc tccagtcagg cagccctana      540
aactggggaa aaaagaaaag gacgccccan cccccagctg tgcanctacg cacctcaaca      600
gcacagggtg gcagcaaaaa aaccacttta ctttggcaca acaaaaaact ngggggggca      660
acccgggcac ccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca      720
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&lt;210&gt; 12

&lt;211&gt; 751

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(751)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 12

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gccccaatc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa      60
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cnccggctgc gatgaagaaa tnacccncg ttgacaaact tgcatggcac tggganccac      540
agtggccna aaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgcccactg      600
ccaacagggg ctgcccacn cncnnaacga tganccnatt gnacaagatc tncntggtct      660
tnatnaacnt gaacctgcn tngtggctcc tgttcaggnc cnnggcctga cttctnaann      720
aangaactcn gaagncccca cngganann g      751

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&lt;210&gt; 13

&lt;211&gt; 729

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(729)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 13

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tgtggancct	cagcagtncc	ctctttcaga	actcantgcc	aagancctg	aacaggagcc	120
accatgcagt	gcttcagctt	cattaagacc	atgatgatcc	tcttcaattt	gtcatcttt	180
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gaagantcac	ctacttcaaa	gaaaaanagt	cctttccccc	atttctgttg	caattgacaa	660
acgtccccaa	cacagccaat	tgaaaacctg	cacccaaccc	aaanggtcc	ccaaccanaa	720
attnaaggg						729

&lt;210&gt; 14

&lt;211&gt; 816

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (816)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 14

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caancttggt	tggatncgaa	gcnaaatct	ncnttctgc	ttgggtggaca	gcaccantna	600
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cacaaccctn	ccccaccac	gggttcngnt	ggttng			816

&lt;210&gt; 15

&lt;211&gt; 783

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (783)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 15

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tcccacgctg	gtactatgac	cccacggagc	agatctgcaa	gagtttctgt	tatggaggct	360



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tgcaaggtgg gcctttgana ngcanctctg gggctcangc gactttcccc cagggcccct 480  
ccatggaaag gcgccatoca ntgttctctg gcacctgtca gcccaccag ttccgtgca 540  
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cncctccntt ttcccnntn aacaaagggc nctngenttt gaactgcccn aaccnaggaa 720  
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ccc 783

<210> 16

<211> 801

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (801)

<223> n = A,T,C or G

<400> 16

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aagtagggtg agtccctcaa atccgtatag ttgggtgaagc cacagcactt gagcccttct 240  
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ggcactacca gcaacgtcag gaagtgtca gccattgtgg tgtacacca ggcgaccaca 360  
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca 420  
cacttgtctc ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg 480  
cncgtgcga atgaaagaaa ntaccacagt tgacaaactg catggccact ggacgacagt 540  
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cnacagggc gncncncn gaaagaatga gccattgaag aaggatontc ntggtcttaa 660  
tgaactgaaa ccttgcattg tggccctgt tcagggtctt tggcagtga ttctganaaa 720  
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<210> 17

<211> 740

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (740)

<223> n = A,T,C or G

<400> 17

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agccaccatg cagtgttca gcttcattaa gaccatgatg atcctcttca atttgcctat 180  
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tgctgaagtt gcagctgctg tggctgcctt ggtgtacacc acaatggctg aaccattcct 480  
gacgttgcgt gtantgcctg ccatcaanaa agattatggg ttcccaggaa aaattcactc 540  
aantntggaa caccnccatg aaaagggctc caatttctgn tggcttcccc aactataccg 600  
gaattttgaa agantcnccc tacttccaaa aaaaaanant tgcctttnc ccenttctgt 660  
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caaaaaaant nnaagggttn

740

<210> 18  
 <211> 802  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(802)  
 <223> n = A,T,C or G

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 acccttnncg ttaccttggg ccaaaccntn centgtgtcg anatngtnaa tcnggnccna 780  
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<210> 19  
 <211> 731  
 <212> DNA  
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<220>  
 <221> misc\_feature  
 <222> (1)...(731)  
 <223> n = A,T,C or G

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 catgcccagn gttanataac nggcnagag tnannttggc tctcccttcc ggctgcgcan 360  
 cngtntgct tagnggacat aacctgacta cttaactgaa cccnngaate tnccnccct 420  
 ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgetcaagta 480  
 aagtgtaccc catncccaat gntgtctnga ngctctgncc tgcnttangt tgggtcctgg 540  
 gaagacctat caattnaagc tatgtttctg actgcctctt gtcacctgna acaancnacc 600  
 cncnntcca agggggggnc ggcccccaat ccccccaacc ntnaattnan tttancccn 660  
 ccccnnggcc cggcctttta cnancntcnn nnacngggna aaaccnnngc tttncccaac 720  
 nnaatccncc t 731

<210> 20  
 <211> 754  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(754)  
 <223> n = A,T,C or G

<400> 20  
 .tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60  
 caaccccctc ntccaaatnn ccttttcgg gnggggggttc caaacccaan ttanntttgg 120  
 annttaaatt aaatnttntt tggnggnnna ancnaatgt nangaaagtt naaccanta 180  
 tnancttnaa tncctggaaa cengtnngtt ccaaaaatnt ttaaccctta antccctcgg 240  
 aaatngttna nggaaaaacc aantttctnt aaggttgttt gaaggntnaa tnaaaancec 300  
 nnccaattgt ttttngccac gectgaatta attggnnttc gntgttttcc nttaaaanaa 360  
 ggnnancccc ggttantnaa tccccccnnc cccaattata ccganttttt ttngaattgg 420  
 gancccnccg gaattaacgg ggnnnntccc tnttgggggg cnggnncccc cccntcggg 480  
 ggttngggnc aggnncnaat tgtttaaggg tccgaaaaat cctccnaga aaaaaanctc 540  
 ccaggntgag nntnggggtt nccccccccc cangggccct ctcgnanagt tgggggtttg 600  
 ggggcctggg attttntttc cctntttnc tccccccccc cngggganag aggttngngt 660  
 tttgntcnnn ggccecnccn aaganccttn ccganttnan taaatccnt gcctnggcga 720  
 agtccnttgn agggntaaan ggccecnnn cggg 754

<210> 21  
 <211> 755  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(755)  
 <223> n = A,T,C or G

<400> 21  
 atcancecat gacccnaac nngggaccnc tcanceggnc nnnnacnc cggecnatca 60  
 nngtnagnnc actncnnttn natcacnccc cncnactac gccncnanc cnacgncta 120  
 nncanatncc actganngcg cgangtngan ngagaaanct nataccanag ncaccanacn 180  
 ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnancctc cnaagtattn 240  
 nncnncanat gattttcctn anccgattac cctncccc tancecctcc ccccaacna 300  
 cgaaggcnet ggncnaagg nngcgnccc ccgtagntc cccncaagt cncncncta 360  
 aactcancn nattaacngc ttctngagta tcaactcccc aatctcacc tactcaactc 420  
 aaaaanaten gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480  
 ttagnngtcc ntnaancntc ctaatactc cagctncc tcnccaattt ccnaanggct 540  
 ctttengaca gcatnttttg gttccnntt gggttcttan ngaattgccc ttctngaac 600  
 gggctcntct tttccttcgg ttancctggg tcnncgggc cagttattat tccntttt 660  
 aaattcntnc cntttanttt tggcnttona aacccccggc cttgaaaacg gccccctgg 720  
 aaaagggtgt tttganaaaa tttttgtttt gtcc 755

<210> 22  
 <211> 849  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(849)  
 <223> n = A,T,C or G

<400> 22  
 tttttttttt tttttangtg tngtcgtgca ggtagaggt tactacaant gtgaanacgt 60  
 acgctnggan taangcgacc cgantttctag gannccct aaaatcanac tgtgaagatn 120

atcctgnna	cggaanggtc	accggnngat	nntgctaggg	tgncenctcc	cannncttn	180
cataactcng	nggcctgcc	caccaccttc	ggcgcceng	ngncegggcc	cgggtcattn	240
gnnttaaccn	cactnngcna	ncggtttccn	necccnncng	accnngcgga	tccgggtnc	300
tctgtcttcc	cctgnagncn	anaaantggg	ceneggnccc	ctttaccct	nnacaagcca	360
cngcctcta	ncncngccc	ccctccant	nngggggact	gcnannget	cgttntctng	420
nnaccccnnn	gggtncctcg	gttgctgant	cnaccgnang	ccanggattc	cnaaggaagg	480
tgcgttnttg	ggccctaccc	ttcgctncgg	nnacccttc	ccgacnanga	nccgctccc	540
cncnncgng	cctcncctcg	caacacccgc	netentcngt	neggnnnccc	ccccaccgc	600
nccctcncnc	ngncgnannc	ctcncncnc	gtctcannca	ccaccccgcc	cggccaggcc	660
ntcanccacn	ggnngacnng	nagcncnntc	gcncgcgcg	gcgncncct	cgcncngaa	720
ctncntcngg	ccantnncgc	tcaancncna	cnaaacgcgc	ctgcgcggcc	cgnagcgncc	780
ncctcncga	gtcctcccg	cttcnacc	angnttccn	cgaggacaen	nnacccgcgc	840
nncangegg						849

<210> 23  
 <211> 872  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (872)  
 <223> n = A,T,C or G

<400> 23	
gogcaacta	tactcgctc
tctgacnanc	ccgattnggc
cacacnncan	aganaaatcc
nggcgaatcg	taatnaggcg
ctnccnacc	tactcttcn
tgggttttn	nntgaccgng
nanngcncgc	necccgnnct
accgcattga	ccctcgccnn
tgggnnngcg	tctgcnccgc
ccncgcctc	tennncaenc
cgncgtgncc	cgnccccacc
cnancngncn	gtcanccnag
cgaanantcc	tencntcan
ntctcccccg	ngngcncntc
tnaccnntac	gantnttcgn
gnactcgtgc	gcctcgtcnc
ngatatchan	aagntcganc
netgccttcc	anagtanacn
tgcgcgcga	atntgtcncc
nagctgtcnn	accctngtn
cnneccctcc	ccctntccat
cttgcncnc	ctgtcctntn
ctnccngaaa	ncgnanacgt
gttcccttcn	ncnmettcca
tntectntgc	cccccttnac
nacgntcttc	acaannncct
ggntnnctcc	
nttgacgttg	nggngangtc
ctcngttncc	aacttancaa
ctctgcantg	tntctctgctc
cc	

<210> 24  
 <211> 815  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (815)  
 <223> n = A,T,C or G

<400> 24	
gcatgcaagc	ttgagtattc
nctgncttcc	tgtgtcaaat
tctntcatta	gtaacaantg
cgcattcncn	gencantatn
gcncctgac	tggngagat
aananceccc	cgngnccac
cctaaatanc	ttgggentaat
tanatatgaa	tctnatntga
cctgtcngan	canattccca
ntcnnntnnn	ncaccnncat
ttntntgacc	nacatgttca
ccaagacctc	ctgtggagggt
catggtcnta	
caagannnga	
tnnattncgn	
ctatcctncc	
tcttggattn	

aacctgcgtc	aganncatca	aacntgggaa	accgcgncc	angtnnaagt	ngnnncanan	420
gatcccgctc	aggnttnacc	atcccttcnc	agcgccect	ttngtgcctt	anagnnagc	480
gtgtccnanc	cnetcaacat	ganacgcgcc	agnccanccg	caattnggca	caatgtcgnc	540
gaaccccccta	gggggantna	tncaaanccc	caggattgtc	cncncangaa	atcccnanc	600
ccnccctac	ccncttttg	gacngtgacc	aantcccgga	gtncagtc	ggcngnctc	660
ccccaccggt	nnccntggg	gggtgaanct	cngnntcanc	cngncgaggn	ntcgnaagga	720
accggnccctn	gncggaanng	ancnntcnga	agncccnct	cgtataaacc	cccctcncca	780
nccnacngnt	agntccccc	cngggtncgg	aangg			815

&lt;210&gt; 25

&lt;211&gt; 775

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(775)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 25

ccgagatgtc	tcgtccgtg	gccttagctg	tgctcgcgt	actctctctt	tctggcctgg	60
aggctatcca	gcgtactcca	aagattcagg	tttactcacg	tcattccagca	gagaatggaa	120
agtcaaat	cctgaattgc	tatgtgtctg	ggtttcatcc	atccgacatt	gaanttgact	180
tactgaagaa	tgganagaga	attgaaaaag	tggagcattc	agacttgtct	ttcagcaagg	240
actggtcttt	ctatctcntg	tactacactg	aattcacccc	cactgaaaaa	gatgagtatg	300
cctgcgcgtg	gaaccatgtg	actttgtcac	agcccaagat	agttaagtgg	gatcgagaca	360
tgtaagcagn	cnncatggaa	gtttgaagat	gccgcatttg	gattggatga	attccaaatt	420
ctgcttgctt	gcntttta	antgatatgc	ntatacacc	taccctttat	gncccaaat	480
tgtaggggtt	acatnantgt	tcnctnnga	catgatcttc	ctttataant	ccnccnttcg	540
aattgcccgt	cnccngttn	ngaattgttc	cnnaaccacg	gttggtctcc	ccaggctncc	600
tcttacggaa	gggcctgggc	cnctttncaa	ggttggggga	accnaaaatt	tcnctntngc	660
cncccncca	cnntcttgng	nnccncttt	ggaacccttc	cnatcccttc	tggcctcnna	720
nccttnncta	anaaaacttn	aaancgtngc	naaanntttt	acttccccc	ttacc	775

&lt;210&gt; 26

&lt;211&gt; 820

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(820)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 26

anattantac	agtgtaatct	tttcccagag	gtgtgtanag	ggaacggggc	ctagaggcat	60
cccanagata	netttancca	acagtgcctt	gaccaagagc	tgctgggcac	atttcctgca	120
gaaaagggtg	cgggtcccat	cactctcct	ctcccatagc	catcccagag	gggtgagtag	180
ccatcangcc	ttcgggtgga	gggagtcang	gaaacaacan	accacagagc	anacagacca	240
ntgatgacca	tgggcgggag	cgagcctctt	ccctgnaccg	gggtggcana	nganagccta	300
nctgaggggt	cacactataa	acgttaacga	ccnagatnan	cacctgcctc	aagtgcaccc	360
ttcctacctg	acnaccagng	accnnnaact	gngcctggg	gacagcnctg	ggancagcta	420
acnnagcact	cacctgcccc	cccatggccg	tnccntccc	tggtcctgnc	aagggaagct	480
ccctgttggg	attncgggga	naccaaggga	nnccctcct	ccanctgtga	aggaaaaann	540
gatggaattt	tncccttcg	gcnntcccc	tcttcttta	caagccccc	ntactctc	600
tccctctntt	ntcctgncc	acttttnacc	ccnnnatte	ccttnattga	tcggannctn	660
ganattccac	tnnccctnc	cntcnatcng	naanacnaaa	nactntctna	ccnnggggat	720
gggnccctcg	ntcatcctct	cttttctnct	accnccnntt	ctttgcctct	ccttngatca	780

tccaacntc gntggcentn cccccennn tcctttnecc

820

<210> 27  
 <211> 818  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (818)  
 <223> n = A,T,C or G

<400> 27  
 tctgggtgat ggcctcttcc tctcagga cctctgactg ctctgggcca aagaatctct 60  
 tgtttcttct cegagcccca ggcagcgggtg attcagccct gcccaacctg attctgatga 120  
 ctgcggatgc tgtgacggac ccaaggggca aatagggtcc cagggtccag ggaggggcgc 180  
 ctgctgagca ctccgcgcc tcacctgcc cagccctgc catgagctct gggctgggtc 240  
 tccgcctcca gggttctgct ctccangca ngccancaa ggcgctggg ccacactggc 300  
 ttcttctgct ccctccctg getctganc tctgtcttcc tgtctgtgc angcnccttg 360  
 gatctcagtt tccctcctc anngaactct gttctgann tcttcantta actntgantt 420  
 tatnaccnan tggncgtgnc tgtcnnaact taatgggccc gaccggctaa tccctccctc 480  
 nctcccttcc anttcnnna accngcttnc cntctctcc ccntancccg ccnggggaanc 540  
 ctcttttgc ctnaccang gcnnnaccg ccctnnctn ggggggcnng gtnnctnnc 600  
 ctgntnnccc cctcncnnt tncctctcc cncnncgcn nngcannttc ncngtcccn 660  
 tnnctcttcn ngntcgnaa ngntcncn tnnnnngcn ngntnntn tccctctcnc 720  
 cnnmtgnang tnnntnnnc ncngnncccc nnnnnnnnn nggnntnnn tctnncngc 780  
 cccnncccc ngnattaagg cctcncnct cccgcnc 818

<210> 28  
 <211> 731  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (731)  
 <223> n = A,T,C or G

<400> 28  
 aggaagggcg gagggatatt gtangggatt gagggatagg agnataangg gggaggtgtg 60  
 tccaacatg anggtgnngt tctctttga angagggttg ngtttttann ccnggtgggt 120  
 gattnaaccc cattgtatgg agnnaaagg ttttagggat ttttcggctc ttatcagtat 180  
 ntanattcct gtnaatcgga aaatnatnt tcnncnggaa aatnttgctc ccatccgnaa 240  
 attnctcccg ggtagtgcatt ntnnggggn cngccangtt tcccaggctg ctanaatcgt 300  
 actaaagntt naagtgggan tncaaatgaa aacctnnac agagnatccn taccgactg 360  
 tnnnttncct tcgccctntg actctgcng agcccaatac ccnngngnat gtncccngn 420  
 nngcgcnc tgaaannnc tcnggctnn gancatcang gggtttcgca tcaaaagcnn 480  
 cgtttcncat naaggcactt tngcctcacc caaccnctng ccctcnncca tttngcgcgc 540  
 nggttcnct acgctnntng cncctnnntn ganattttnc ccgcctnggg naancctcct 600  
 gnaatgggta gggnccttntc ttttnaccnn gnggtntact aatcnnctnc acgctnctt 660  
 tctcnacccc ccccttttt caatcccanc ggcnatggg gtctcccn cgangggggg 720  
 nnnccann c 731

<210> 29  
 <211> 822  
 <212> DNA  
 <213> Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (822)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 29

actagtccag	tgtgggtggaa	ttccattgtg	ttgggggnenc	ttctatgant	antnttagat	60
cgctcanacc	tcacancctc	ccnacnangc	ctataangaa	nannaataga	nctgtncnnt	120
atntntacnc	tcatanncct	cnnnaccac	tcctctctaa	ccctactgtg	gcctatngcn	180
tnnctantct	ntgccgcctn	cnanccaccn	gtggggccnac	cncnngnatt	ctcnatctcc	240
tcnccatntn	gcctananta	ngtncatacc	ctatacctac	nccaatgcta	nnnctaancn	300
tccatnantt	annntaacta	ccactgaent	ngaetttcnc	atnanctcct	aatttgaatc	360
tactctgact	cccacngcct	annnattagc	ancntcccc	nacnatntct	caaccaaate	420
ntcaacaacc	tatctanctg	ttcnccaacc	nttnccctcg	atccccnnac	aacccccctc	480
ccaaataccc	nccacctgac	ncctaaccen	caccatcccg	gcaagccnan	ggncatttan	540
ccactggaat	cacnatngga	naaaaaaac	ccnaactctc	tancncnnat	ctcccataana	600
aatnctcctn	naattttactn	ncantnccat	caanccccacn	tgaaacnnaa	cccctgtttt	660
tanatccctt	ctttcgaaaa	ccnacccttt	annncccaac	ctttngggcc	cccccnctnc	720
ccnaatgaag	gnnccccaat	cnangaaacg	ncctngaaaa	ancnaggcna	anannntccg	780
canatcctat	cccttanttn	ggggncctt	nccngggcc	cc		822

&lt;210&gt; 30

&lt;211&gt; 787

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (787)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 30

cggccgcctg	ctctggcaca	tgectcctga	atggcatcaa	aagtgatgga	ctgcccattg	60
ctagagaaga	ccttctctcc	tactgtcatt	atggagccct	gcagactgag	ggctcccctt	120
gtctgcagga	tttgatgtct	gaagtcgtgg	agtgtggctt	ggagctcctc	atctacatna	180
gctggaagcc	ctggaggggc	tctctcgcca	gcctccccct	tctctccacg	ctctccangg	240
acaccagggg	ctccaggcag	cccattatc	ccagnangac	atgggtgttc	tccacgcgga	300
cccatggggc	ctgnaaggcc	agggctctct	ttgacaccat	ctctcccgtc	ctgcctggca	360
ggcctgggga	tccactantt	ctanaacggg	cgccaccncg	gtgggagctc	cagcttttgt	420
tccnttaat	gaaggttaat	tgcnegcttg	gcgtaatcat	nggtcanaac	tntttcctgt	480
gtgaaattgt	ttntccccct	ncnattccnc	ncnacatacn	aacccgggan	cataaagtgt	540
taaagcctgg	gggtngcctn	nngaathnaac	tnaactcaat	taattgcgtt	ggctcatggc	600
ccgctttccn	ttcnggaaaa	ctgtentccc	ctgenttnt	gaatcgggca	ccccccnggg	660
aaaagcggtt	tgctttttng	ggggntcctt	ccncttcccc	cctcnctaan	ccctnccgct	720
cggctcgttc	nggtngcggg	gaangggnat	nnnctcccnc	naagggggng	agnnngntat	780
ccccaaa						787

&lt;210&gt; 31

&lt;211&gt; 799

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (799)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 31

```

tttttttttt tttttttggc gatgetactg ttttaattgca ggaggtgggg gtgtgtgtac      60
catgtaccag ggctattaga agcaagaagg aaggagggag ggcagagcgc cctgctgagc      120
aacaaaggac tcctgcagcc ttctctgtct gtctcttggc gcaggcacat ggggaggcct      180
cccgagggtt gggggccacc agtccagggtt tgggagcact acanggggtg ggagtgggtg      240
gtggctggtn cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca      300
ggggaccttc tgttctccca nggnaacttc nttnatctcn aaagaacaca actgtttctt      360
cngcanttct ggctgttcat ggaaagcaca ggtgtccnat ttnggctggg acttggtaca      420
tatggttccg gccacactct ccntcnaaa aagtaattca ccccccccn cctctnttg      480
cctgggacct taantacca caccggaact canttantta ttcactctng gntgggcttg      540
ntnatncncc cctgaangcg ccaagttgaa aggccacgcc gtncnctc cccatagnan      600
nttttnnccn canctaagc cccccnggc aacnatccaa tcccccccn tgggggcccc      660
agcccanggc ccccgntcgc ggnnnccngn cncgnantcc ccaggntctc ccantcngnc      720
ccnnngcncc cccgcacgca gaacanaagg ntngagccnc cgcannnnnn nggtnnncac      780
ctcgcceccc ccnnngnng

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<210> 32
<211> 789
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(789)
<223> n = A,T,C or G

```

```

<400> 32
tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt      60
ttttnccnag ggcaggttta ttgacaacct cncgggacac aancaggctg gggacaggac      120
ggcaacaggc tccggcggcg gcggcgcgcg cctacactgc ggtaccaaata ntgcagcctc      180
cgctcccgcg tgatnttccg ctgcagctgc aggatgcctt aaaacagggc ctgggcntn      240
ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc      300
nattaggaat agtggtnnta ccnccnccg ttggcncact cccnttgaa accacttntc      360
ggggtcccg catctggtct taaaccttgc aaacnctggg gccctctttt tggttantnt      420
ncngccaca atcatnactc agactggcnc gggctggccc caaaaaancc ccccaaaacc      480
ggncatgtc ttncgggggt tgcctgnatn tncatcacct cccgggcnca ncaggncac      540
ccaaaagttc ttngggcccn caaaaaanct ccggggggnc ccagtttcaa caaagtcac      600
cccttgggcc cccaaatcct cccccgntt nctgggtttg ggaacccacg cctctnctt      660
tggnnggcaa gntggntccc ccttcgggccc cccggtgggc ccnctctaa ngaaaacncc      720
ntcctnnnca ccatccccc nngnnacgnc tancaangna tccctttttt tanaaacggg      780
ccccccnng

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<210> 33
<211> 793
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(793)
<223> n = A,T,C or G

```

```

<400> 33
gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg      60
aattcatggc tgttggagca atanaacccc agttctacga gctgctgatc aaaggacttg      120
gactaaagtc tgatgaactt ccaatcaga tgagcatgga tgattggcca gaaatgaana      180
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg      240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttgttcat catgatcaca      300
acaangaacg gggctcggtt atcaccantg aggagcagga cgtgagcccc cgccctgcac      360

```



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ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc 420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct 480
tggegtaatc atggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac 540
acaacatacg anccggaagc atnaaatttt aaagcctggn ggtngcctaa tgantgaact 600
nactcacatt aattggcttt gcgctcaactg cccgctttcc agtccggaaa acctgtcctt 660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggengtttg cttnttgggg 720
cgencttccc gctttctcgc ttctgaant ccttcccccc ggtctttcgg cttgcggnca 780
acggtatena cct 793

```

&lt;210&gt; 34

&lt;211&gt; 756

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(756)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 34

```

gcgcgaccg gcatgtacga gcaactcaag ggcgagtggg accgtaaaag ccccaatctt 60
ancaagtgcg gggaanagct gggctcgactc aagctagtgc ttctggagct caacttcttg 120
ccaaccacag ggaccaagct gaccaaagcag cagctaattc tggcccgta catactggag 180
atcgggggccc aatggagcat cctacgcaan gacatccctt ccttcgagcg ctacatggcc 240
cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac 300
cagctcttgg gctcaacct cctcttcttg ctgtcccaga accgggtggc tgantnccac 360
acgganttgg ancggtgccc tgcccaanga catacanacc aatgtctaca tcnaccacca 420
gtgtccttga gcaatactga tgganggcag ctaccncaaa gtnttcttgg ccnagggtta 480
catccccgc cgagagctac accttcttca ttgacatcct gctcgacact atcagggtat 540
aaaatcgng ggttgctcca gaaaggctnc aanaanatcc ttttctctga agggccccgg 600
atnctnctagt nctagaatcg gcccgccatc gcggtgganc ctccaacctt tcgttncct 660
ttactgaggg ttnattgccg cccttgccgt tatcatggtc acnccngtn cctgtgttga 720
aattnttaac cccccacaat tccacgcena cattng 756

```

&lt;210&gt; 35

&lt;211&gt; 834

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(834)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 35

```

ggggatctct anactnacct gnatgcatgg ttgtcggtgt ggtcgctgtc gatgaanatg 60
aacaggatct tgccettgaa gctctcggt gctgtnttta agttgctcag tctgccgtca 120
tagtcagaca cnetcttggg caaaaaacan caggatntga gtcttgattt cacctccaat 180
aatcttcngg gctgtctgct cggtgaaact gatgacnang ggcagctggt tgtgtntgat 240
aaantccanc angttctcct tggtagctc ccttcaaaag ttgttccggc cttcatcaaa 300
cttctnnaan angannance canctttgtc gagctggnat ttgganaaca cgtcactgtt 360
ggaaactgat cccaaatggt atgtcatcca tcgctctgct tgcttgcaaa aaacttgctt 420
ggcncaaact cgactcccn tccttgaaag aagccnatca cccccctc cctggactcc 480
nncaangact ctncgctnc ccntccnng cagggttggg ggcanccgg gccntgcgc 540
ttcttcagcc agttcacnat nttcatcage cctctgcca gctgtntat tccttggggg 600
ggaanccgtc tctcccttcc tgaannaact ttgaccgtng gaatagccg gontcncnt 660
acntnctggg ccgggttcaa antccctcct ttgnenctn cctcgggcca ttctggattt 720
nccnaacttt ttcttcccc cncctcncgg ngtttggntt tttcatnggg ccccaactct 780

```

gctnttggcc antcccctgg gggcntntan cccccctnt ggtcccntng ggcc

834

<210> 36  
 <211> 814  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(814)  
 <223> n = A,T,C or G

<400> 36  
 cgngcgttt cngccgcgc cccgtttcca tgacnaagge tcccttcang ttaaatacnn 60  
 cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgcccc 120  
 naacgccaac tcaggccatt cctaccaaag gaagaaagge tggctctccc accccctgta 180  
 ggaaaggcct gccttgtaag acaccacaat ncggctgaat ctnaagtctt gtgttttact 240  
 aatggaaaaa aaaaaataac aanagggttt gttctcatgg ctgcccaccg cagcctggca 300  
 ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgetctt ttggacatca 360  
 ggcttgatgg tatcactgcc acntttccac ccagctgggc ncccttcccc catntttgtc 420  
 antganctgg aaggcctgaa ncttagtctc caaaagtctc ngcccacaag accggccacc 480  
 aggggangtc ntttncagtg gatctgccaa anantaccn tatcatcnnt gaataaaaaag 540  
 gccctgaac ganatgcttc cancanctt taagacccat aatcctngaa ccatggtgcc 600  
 cttccggctc gatccnaaag gaatgttcct gggcccant cctcctttg ttncttacgt 660  
 tgtnttgga cctgtctngn atnaccaan tganateccc ngaagcacc tncctctggc 720  
 atttganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcncnaa 780  
 ngngaactca agaaggtctn ngaaaaacca cncn 814

<210> 37  
 <211> 760  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(760)  
 <223> n = A,T,C or G

<400> 37  
 gcatgctgct cttcctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg 60  
 gcgcagtgtt cgctgaagggt gttgtagtac cagcgcggga tgctctcctt gcagagtcct 120  
 gtgtctggca ggtccacgca atgccctttg tcaactggga aatggatgcg ctggagctcg 180  
 tenaanccac tcgtgtattt ttcacangca gcctcctccg aagcctccgg gcagttgggg 240  
 gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt 300  
 gggctgacag gtgccagaac acactggatn ggcctttcca tggaagggcc tgggggaaat 360  
 cncctnancc caaactgcct ctcaaaggcc acctgcaca ccccgacagg ctagaaatgc 420  
 actcttcttc ccaaaggtag ttgttcttgt tgcccagca ncctccanca aaccaaanc 480  
 ttgcaaaatc tgctccgtgg gggcatnnn taccanggtt ggggaaanaa acccgcnng 540  
 gancncctt gtttgaatgc naaggnaata atcctcctgt cttgcttggg tggaanagca 600  
 caattgaact gttaacnttg ggccnggttc cncctnggtg gtctgaaact aatcacgcgc 660  
 actggaaaaa ggtangtgc ttccttgaat tcccaaantt cccctngntt tgggtnttt 720  
 ctctctncc ctaaaaatcg tnttcccccc cntanggcg 760

<210> 38  
 <211> 724  
 <212> DNA  
 <213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(724)  
<223> n = A,T,C or G

<400> 38  
tttttttttt tttttttttt tttttttttt tttttaaaaa cccctcccat tgaatgaaaa 60  
cttcnnaaat tgtccaaccc cctennccaa atnnccattt ccgggggggg gttccaaacc 120  
caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa 180  
aatttaaccc attatnaact taaatncctn gaaaccctg gnttccaaaa atttttaacc 240  
cttaaatecc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaagggt 300  
ngattttaaac ccccttnant tnttttnacc cnngnctnaa ntatttngnt tccggtgttt 360  
tcctnttaan cntnggtaac tcccgnataat gaannnccct aanccaatta aaccgaattt 420  
tttttgaatt ggaaattccn ngggaattna ccgggggttt tcccntttgg gggccatncc 480  
ccncttttcg ggggttgggn ntagggtgaa tttttnnang ncccaaaaaa nccccaana 540  
aaaaaactcc caagnnttaa ttngaattnc ccccttccca ggccttttgg gaaaggnggg 600  
ttnttggggg ccngggantt cnttccccc ttnccncccc cccccnggt aaanggttat 660  
ngnntttggt ttttgggcc cttnanggac cttccggatn gaaattaaat ccccggnccg 720  
gccg 724

<210> 39  
<211> 751  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(751)  
<223> n = A,T,C or G

<400> 39  
tttttttttt tttttctttg ctcacattta atttttattt tgattttttt taatgctgca 60  
caacacaata tttatttcat ttgtttcttt tatttcattt tatttgttg ctgctgctgt 120  
tttatttatt tttactgaaa gtgagaggga acttttgtgg ccttttttcc tttttctgta 180  
ggccgcctta agctttctaa atttggaaca tctaagcaag ctgaanggaa aagggggttt 240  
cgcaaatca ctcgggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300  
ttaactgctt gtacaattac ntttacttt taattaattg tgctnaange ttaattana 360  
cttgggggtt ccttccccc accaaccnccn ctgacaaaaa gtgcengccc tcaaatnatg 420  
tcccgcnnt cnttgaaaca cacngcngaa ngttctcatt ntcccnccn caggtnaaaa 480  
tgaagggtta ccatntttta cncacctcc acntggcnnn gctgaatcc tcnaaaanccn 540  
cctcaanccn aattnctnng ccccggtcnc gentnngtec cncctgggt ccgggaantn 600  
caccccnnga annenntnnc naacnaaatt ccgaaaatat tcccnntcnc tcaattcccc 660  
cnnagactnt cctcnncnccn cncaatttcc tttntntcac gaacnccncc cnnaaatgn 720  
nnnncnctc cncnngtcn naatcnccan c 751

<210> 40  
<211> 753  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(753)  
<223> n = A,T,C or G

<400> 40  
gtggtatttt ctgtaagatc aggtgttccct cctcgtagg ttttagaggaa acaccctcat 60  
agatgaaaac cccccgaga cagcagcact gcaactgccca agcagccggg gtaggagggg 120

```

cgccctatgc acagctgggc ccttgagaca gcagggcttc gatgtcagge tcgatgtcaa 180
tggtctggaa gcggcggtg tacctgcgta ggggcacacc gtcagggccc accaggaact 240
tctcaaagtt ccaggcaacn tcgttgcgac acaccggaga ccagggtgatn agcttggggt 300
cggtcataa cgcgggtggcg tcgtcgctgg gagctggcag ggctcccgcc aggaaggcna 360
ataaaagggt cgcggcgca cgttcantc cgcacttctc naanaccatg angttggggt 420
cnaaccacc accannccg acttccttga nggaattccc aaatctcttc gntcttgggc 480
ttctnctgat gccctantg gttgccnngn atgccaanca nccccaancc cgggggtcct 540
aaanaccn cctctentt tcatctgggt tntntcccc ggacctgggt tctctcaag 600
gganccata tctcnaccn tactcaccnt nccccccnt gnnaccanc cttctanngn 660
ttccncccg nctctggcc ontcaaan gcttnacna cctgggtctg ccttcccccc 720
tnccctatct gnaccnccn tttgtctcan tnt 753

```

<210> 41  
 <211> 341  
 <212> DNA  
 <213> Homo sapien

```

<400> 41
actatatcca tcacaacaga catgcttcat cccatagact tcttgacata gcttcaaagt 60
agtgaacca tccttgattt atatacatat atgttctcag tattttggga gcctttccac 120
ttctttaaac cttgttcatt atgaacctg aaaataggaa tttgtgaaga gttaaaaagt 180
tatagcttgt ttacgtagta agtttttgaa gtctacattc aatccagaca cttagttgag 240
tgtaaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat 300
ttttactttt tgattaattg tgttttatat attagggtag t 341

```

<210> 42  
 <211> 101  
 <212> DNA  
 <213> Homo sapien

```

<400> 42
acttactgaa tttagttctg tgctcttctt tatttagtgt tgtatcataa atactttgat 60
gtttcaaaca ttctaaataa ataattttca gtggcttcat a 101

```

<210> 43  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

```

<400> 43
acatctttgt tacagtctaa gatgtgttct taaatcacca ttccttctg gtcctcacc 60
tccaggggtg tctcactg taattagagc tattgaggag tctttacagc aaattaagat 120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaaccca 180
cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat 240
tggtacaga acgagagtta tcttgataa ctcagagctg agtacctgcc cgggggccc 300
tcgaa 305

```

<210> 44  
 <211> 852  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (852)  
 <223> n = A,T,C or G

<400> 44

```

acataaatat cagagaaaag tagtctttga aatatttacg tccaggagtt ctttgtttct    60
gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt    120
ctctccatcc tcgggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct    180
ccagaatttc tctttttag tagtatctca tagctcggct gagcttttca taggtcatgc    240
tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga    300
agacgccctc agatcgggtc tcccatttta ttaatcctgg gttcttgtct gggttcaaga    360
ggatgtcgcg gatgaattcc cataagttag tccctctcgg gttgtgcttt ttgggtgtggc    420
acttggcagg ggggtcttgc tcctttttca tatcagggtga ctctgcaaca ggaagggtgac    480
tggtgtgtgt catggagatc tgagcccggc agaaagtttt gctgtccaac aaatctactg    540
tgctaccata gttggtgtca tataaatagt tctngtcttt ccagggtgtc atgatggaag    600
gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tcactactgc    660
actggccgtt ccacttcaga tgctgcaagt tgctgtagag gagntgccc gccgtccctg    720
ccgccgggt gaactcctgc aaactcatgc tgcaaagggt ctcgccgttg atgtcgaaact    780
cntggaaagg gatacaattg gcatccagct ggttgggtgc caggaggtga tggagccact    840
ccacacctg gt                                     852

```

&lt;210&gt; 45

&lt;211&gt; 234

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 45

```

acaacagacc cttgctcgct aacgacctca tgctcatcaa gttggacgaa tccgtgtccg    60
agtctgacac catccggagc atcagcattg cttcgcagtg ccctaccgcg gggaactctt    120
gctcgttttc tggctggggg ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg    180
tgaacgtgtc ggtggtgtct gaggaggtct gcagtaagct ctatgaccgg ctgt       234

```

&lt;210&gt; 46

&lt;211&gt; 590

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(590)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 46

```

actttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atggtgtgta    60
atttgatagc aatatttttg agattacaga gttttagtaa ttaccaatta cacagttaaa    120
aagaagataa tatattccaa gcanatacaa aatatctaata gaaagatcaa ggcaggaaaa    180
tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta    240
aaagctttca aaanaanaaa ttattgcagt ctanttaatt caaacagtgt taaatgggtat    300
caggataaan aactgaaggg canaaagaat taattttcac ttcatgtaac ncaccanant    360
ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggtctttc    420
tggtctctaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag    480
ggctcctggt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct    540
gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt       590

```

&lt;210&gt; 47

&lt;211&gt; 774

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(774)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 47

```

acaagggggc ataatgaagg agtggggana gatttttaaag aaggaaaaaa aacgaggccc      60
tgaacagaat tttcctgnac aacggggctt caaaataatt ttcttgggga ggttcaagac      120
gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg      180
cattacagac gggactctgg gaggaaggat aaacagaaag gggacaaagg ctaatcccaa      240
aacatcaaaag aaagggaagg ggcgtcatac ctcccagcct acacagttct ccagggtctt      300
cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctctgtgtg      360
ctggctcctg gtcttcagcc cccagctctg gaagccacc ctctgctgat cctgcgtggc      420
ccacactcct tgaacacaca tccccaggtt atattcctgg acatggctga acctcctatt      480
cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc      540
acggcatggg aagcctttct gacttgcttg attactccag catcttggaa caatccctga      600
ttcccactc cttagaggca agataggggt gttaagagta gggctggacc acttggagcc      660
aggctgctgg cttcaaattn tggctcattt acgagctatg ggaccttggg caagtnatct      720
tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt          774

```

&lt;210&gt; 48

&lt;211&gt; 124

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(124)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 48

```

canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt      60
ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact      120
tggt                                              124

```

&lt;210&gt; 49

&lt;211&gt; 147

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(147)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 49

```

gccgatgcta ctattttatt gcaggaggtg ggggtgtttt tattattctc tcaacagctt      60
tgtggctaca ggtgggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt      120
ttagggcacc catatcccaa gcantgt                      147

```

&lt;210&gt; 50

&lt;211&gt; 107

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 50

```

acattaaatt aataaaagga ctgttggggt tctgctaaaa cacatggctt gatatatattgc      60
atgggtttgag gttaggagga gttaggcata tgttttggga gaggggt                      107

```

&lt;210&gt; 51

&lt;211&gt; 204

&lt;212&gt; DNA

<213> Homo sapien

<400> 51

gtcctaggaa gtctagggga cacacgactc tgggggtcacg gggccgacac acttgacagg	60
cgggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaaag gaaaatcaag	120
gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgccc cacttgacca	180
cctccctttt gggaccagca atgt	204

<210> 52

<211> 491

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (491)

<223> n = A,T,C or G

<400> 52

acaaagataa catttatctt ataacaaaaa tttgatagtt ttaaagggtta gtattgtgta	60
gggtattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca	120
ccatcagaca gggtttttaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa	180
aaaacttctt gtatcaattt cttttgttca aaatgactga cttaantatt tttaaatatt	240
tcanaaacac ttctcaaaaa attttcaana tggtagcttt canatgtnc ctcagtccca	300
atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc	360
atgcaacagt gtcttttctt tnttttttct tttttttttt ttacaggcac agaaactcat	420
caattttatt tggataacaa aggggtctcca aatttatattg aaaaataaat ccaagttaat	480
atcactcttg t	491

<210> 53

<211> 484

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (484)

<223> n = A,T,C or G

<400> 53

acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga	60
gtattaacag ttgctgaagt ttggattttt tatgcagcat tttctttttg ctttgataac	120
actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct	180
caatcaaate tctacataac actatagtaa ttaaaacggt aaaaaaaagt gttgaaatct	240
gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc	300
agcttttgant ttctttgtgc tgatangagg aaaggctgaa ttaccttggt gcctctccct	360
aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncg	420
tancttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc	480
cant	484

<210> 54

<211> 151

<212> DNA

<213> Homo sapien

<400> 54

actaaacctc gtgcttgta actccatata gaaaacggtg ccatccctga acacggctgg	60
ccactgggta tactgctgac aaccgcaaca aaaaaaacac aaatccttgg cactggctag	120

tctatgtcct ctcaagtgcc tttttgtttg t 151

<210> 55  
<211> 91  
<212> DNA  
<213> Homo sapien

<400> 55  
acctggcttg tctccgggtg gttcccggcg cccccacgg tccccagaac ggacactttc 60  
gccctccagt ggatactga gccaaagtgg t 91

<210> 56  
<211> 133  
<212> DNA  
<213> Homo sapien

<400> 56  
ggcggatgtg cggttggtat atacaaatat gtcattttat gtaagggact tgagtatact 60  
tggatttttg gtatctgtgg gttgggggga cggtcagga accaataccc catggatacc 120  
aagggacaac tgt 133

<210> 57  
<211> 147  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(147)  
<223> n = A,T,C or G

<400> 57  
actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gngtgggcgc 60  
gactgggagc tgagcccttc cctttgcgcc tgcctcagag gattgttgcc gacntgcana 120  
tctcantggg ctggatncat gcagggt 147

<210> 58  
<211> 198  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(198)  
<223> n = A,T,C or G

<400> 58  
acagggatat aggtttnaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc 60  
tgattacata catttacct ttaaaaaaga tgtaaatctt aatttttatg ccatctatta 120  
atttaccaat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt 180  
ttgacttcta agtttggg 198

<210> 59  
<211> 330  
<212> DNA  
<213> Homo sapien

<400> 59



acaacaaatg ggttgtgagg aagtcttatac agcaaaactg gtgatggcta ctgaaaagat	60
ccattgaaaa ttatcattaa tgatttttaa tgacaagtta tcaaaaactc actcaatttt	120
cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atcttctgaa	180
tacagtcaat aaatgacaaa gccagggcct acaggtggtt tccagacttt ccagaccag	240
cagaaggaat ctattttatc acatggatct ccgtctgtgc tcaaaatacc taatgatatt	300
tttcgtcttt attggacttc tttgaagagt	330

<210> 60  
 <211> 175  
 <212> DNA  
 <213> Homo sapien

<400> 60	
accgtgggtg cttctacat tcttgacggc tcttcacca acatctggtt ctacttcggc	60
gtcgtgggct cttctctctt catcctcctc cagctggtgc tgctcatcga ctttgcgac	120
tcttggaacc agcgggtggct gggcaaggcc gaggagtgcg attcccgtgc ctggt	175

<210> 61  
 <211> 154  
 <212> DNA  
 <213> Homo sapien

<400> 61	
accccacttt tctcctgtg agcagtctgg acttctcact gctacatgat gagggtgagt	60
ggttggtgct cttcaacagt atcctcccct ttccggatct gctgagccgg acagcagtgc	120
tggactgcac agccccgggg ctccacattg ctgt	154

<210> 62  
 <211> 30  
 <212> DNA  
 <213> Homo sapien

<400> 62	
cgctcgagcc ctatagttag tcgtattaga	30

<210> 63  
 <211> 89  
 <212> DNA  
 <213> Homo sapien

<400> 63	
acaagtcatt tcagcaccct ttgctcttca aaactgacca tcttttatat ttaatgttc	60
ctgtatgaat aaaaatggtt atgtcaagt	89

<210> 64  
 <211> 97  
 <212> DNA  
 <213> Homo sapien

<400> 64	
accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa gggtctgcag	60
aatcagtgc aatcaggattg gtccttggat ctggggg	97

<210> 65  
 <211> 377  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(377)  
 <223> n = A,T,C or G

<400> 65  
 acaacaanaa ntcccttctt taggccaactg atggaaacct ggaacccccct tttgatggca 60  
 gcatggcgctc ctaggccttg acacagcggc tggggtttg gctntcccaa accgcacacc 120  
 ccaaccctgg tctaccacaca nttctggcta tgggctgtct ctgccactga acatcagggg 180  
 tcggtcataa natgaaatcc caanggggac agaggtcagt agagggaagct caatgagaaa 240  
 ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg 300  
 tgggggtgaa ctacccccc gaggaatcat gctggggcga tgcaanggtg ccaacaggag 360  
 gggcgggagg agcatgt 377

<210> 66  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 66  
 acgcctttcc ctcagaattc agggaagaga ctgtgcctg ccttcctccg ttgttgcgtg 60  
 agaaccctgt tgccccctcc caccatatcc accctcgctc catctttgaa ctcaaacacg 120  
 aggaactaac tgcaccctgg tctctcccc agtccccagt tcacctcca tccctcacct 180  
 tctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggttt 240  
 ttatatattt ttttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac 300  
 tgttt 305

<210> 67  
 <211> 385  
 <212> DNA  
 <213> Homo sapien

<400> 67  
 actacacaca ctccacttgc ccttgtgaga cactttgtcc cagcacttta ggaatgctga 60  
 ggtcggacca gccacatctc atgtgcaaga ttgcccagca gacatcaggt ctgagagttc 120  
 cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc 180  
 tgtgtgtgctc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg 240  
 ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg 300  
 cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgcccatac 360  
 catagtttct gtgctagtgg accgt 385

<210> 68  
 <211> 73  
 <212> DNA  
 <213> Homo sapien

<400> 68  
 acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa 60  
 gtttttttaa tgg 73

<210> 69  
 <211> 536  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(536)

<223> n = A,T,C or G

<400> 69

actagtccag	tgtggtggaa	ttccattgtg	ttggggggtc	tcaccctcct	ctcctgcagc	60
tccagctttg	tgctctgcct	ctgaggagac	catggcccag	catctgagta	ccttgcctgt	120
cctgctggcc	accctagctg	tggccctggc	ctggagcccc	aaggaggagg	ataggataat	180
cccgggtggc	atctataacg	cagacctcaa	tgatgagtgg	gtacagcgtg	cccttcactt	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgtc	cgctgcgggt	300
actaagagcc	aggcaacaga	ccgttggggg	ggtgaattac	ttcttcgacg	tagagggtgg	360
ccgaaccata	tgtaccaagt	cccagcccaa	cttgacacc	tgtgccttcc	atgaacagcc	420
agaactgcag	aagaaacagt	tgtgctcttt	cgagatctac	gaagtccct	ggggagaaca	480
gaangtccct	gggtgaaatc	caggtgtcaa	gaaatcctan	ggatctgttg	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgaccccta	acagggggcc	tctcagccct	cctaattgacc	tccggcctag	ccatgtgatt	60
tcacttccac	tccataacgc	tcctcatact	aggcctacta	accaacacac	taaccatata	120
ccaatgatgg	cgcgatgtaa	cacgagaaaag	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggg	cttcgatacg	ggataatcct	attttattacc	tcagaagttt	ttttcttcgc	240
agggtatttt	ctgagccctt	taccactcca	gcttagcccc	taccccccaa	ctaggagggc	300
actggccccc	aacaggcatc	accccgttaa	atcccctaga	agtcccactc	ctaaacacat	360
ccgtattact	cgcacagga	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aattattcaa	agcactgctt	attacaattt	tactgggtct	ctatttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (533)

<223> n = A,T,C or G

<400> 71

agagctatag	gtacagtgtg	atctcagctt	tgcaaacaca	ttttctacat	agatagtact	60
aggtattaat	agatatgtaa	agaaagaaat	cacaccatta	ataatggtaa	gattgggtta	120
tgtgatttta	gtggtatttt	tggcaccctt	atatatgttt	tcctaaacttt	cagcagtgtat	180
attatttcca	taacttaaaa	agtgagtgtg	aaaaagaaaa	tctccagcaa	gcatctcatt	240
taaataaagg	tttgtcatct	ttaaaaatac	agcaatatgt	gactttttta	aaaagctgtc	300
aaataggtgt	gaccctacta	ataattatta	gaaatacatt	taaaaacatc	gagtacctca	360
agtcagtttg	ccttgaaaaa	tatcaaatat	aactcttaga	gaaatgtaca	taaaagaatg	420
cttcgtaatt	ttggagtang	aggttccctc	ctcaattttg	tattttttaa	aagtacatgg	480
taaaaaaaaa	aattcacaca	agtatataag	gctgtaaaaa	gaagaattct	gcc	533

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (511)

<223> n = A,T,C or G

&lt;400&gt; 72

tattacggaa	aaacacacca	cataattcaa	ctancaaaga	anactgcttc	agggcggtgta	60
aatgaaaagg	cttccaggca	gttatctgat	taaagaacac	taaaagaggg	acaaggctaa	120
aagccgcagg	atgtctacac	tatancaggc	gctatttggg	ttggctggag	gagctgtgga	180
aaacatggan	agattgggtc	tgganatcgc	cgtggctatt	cctcattgtt	attacanagt	240
gaggttctct	gtgtgcccac	tggtttgaaa	accgttctnc	aataatgata	gaatagtaca	300
cacatgagaa	ctgaaatggc	ccaaacccag	aaagaaagcc	caactagatc	ctcagaanac	360
gcttctaggg	acaataaccg	atgaagaaaa	gatggcctcc	ttgtgcccc	gtctgttatg	420
atttctctcc	attgcagcna	naaacccgtt	cttctaagca	aacncagggtg	atgatggcna	480
aaatacaccc	cctcttgaag	naccnggagg	a			511

&lt;210&gt; 73

&lt;211&gt; 499

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(499)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 73

cagtgccagc	actggtgcc	gtaccagtac	caataacagt	gccagtgcc	gtgccagcac	60
cagtgggtgc	ttcagtgtg	gtgccagcct	gaccgccact	ctcacatttg	ggctcttcgc	120
tggccttgg	ggagctggg	ccagcaccag	tggcagctct	gggtgcctgtg	gtttctccta	180
caagtgtgat	tttagatatt	gttaatcctg	ccagtctttc	tcttcaagcc	aggggtgcac	240
ctcagaaacc	tactcaacac	agcactctag	gcagccacta	tcaatcaatt	gaagttgaca	300
ctctgcatta	aatctatttg	ccatttctga	aaaaaaaaaa	aaaaaaagg	cggccgctcg	360
antctagagg	gcccgtttta	acccgctgat	cagcctcgac	tgtgccttct	anttgccagc	420
catctgttgt	ttgcccctcc	cccngtgcct	tccttgaccc	tggaaagtgc	cactccact	480
gtcctttcct	aantaaaaat					499

&lt;210&gt; 74

&lt;211&gt; 537

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(537)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 74

tttcatagga	gaacacactg	aggagatact	tgaagaattt	ggattcagcc	gcgaagagat	60
ttatcagctt	aactcagata	aaatcattga	aagtaataag	gtaaaagcta	gtctctaact	120
tccaggccca	cggctcaagt	gaatttgaat	actgcattta	cagtgtagag	taacacataa	180
cattgtatgc	atggaaacat	ggaggaacag	tattacagtg	tcctaccact	ctaatcaaga	240
aaagaattac	agactctgat	tctacagtga	tgattgaatt	ctaaaaatgg	taatcattag	300
ggcttttgat	ttataanact	ttgggtactt	atactaaatt	atggtagtta	tactgccttc	360
cagtttgctt	gatataattg	ttgatattaa	gattcttgac	ttatatattg	aatgggttct	420
actgaaaaan	gaatgatata	ttcttgaaga	catcgatata	cattttattta	cactcttgat	480
tctacaatgt	agaaaatgaa	ggaaatgccc	caaattgtat	ggtgataaaa	gtcccgt	537

&lt;210&gt; 75

&lt;211&gt; 467

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(467)  
 <223> n = A,T,C or G

<400> 75  
 caaanacaat tgttcaaaaag atgcaaatga tacactactg ctgcagctca caaacacctc 60  
 tgcattattac acgtacctcc tctgtctcct caagtagtgt ggtctatattt gccatcatca 120  
 cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180  
 tggcacaagg aggccatctt tctctcatcg gttattgtcc ctagaagcgt cttctgagga 240  
 tctagttggg ctttctttct gggtttgggc catttcantt ctcagtgtgt tactattcta 300  
 tcattattgt ataacgggtt tcaaaccngt gggcacncag agaacctcac tctgtaataa 360  
 caatgaggaa tagccacggg gatctccagc accaaatctc tccatgtnt tccagagctc 420  
 ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 467

<210> 76  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(400)  
 <223> n = A,T,C or G

<400> 76  
 aagctgacag cattcggggc gagatgtctc gctccgtggc cttagctgtg ctgcgcgtac 60  
 tctctctttc tggcctggag gctatccagc gtactccaaa gattcagggt tactcacgtc 120  
 atccagcaga gaatggaaaag tcaaatttcc tgaattgcta tgtgtctggg ttctcatccat 180  
 ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaaagt gagcattcag 240  
 acttgtcttt cagcaaggac tgggtctttct atctcttgta ctacactgaa ttcaccccca 300  
 ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360  
 ttnagtggga tcganacatg taagcagcan catgggaggt 400

<210> 77  
 <211> 248  
 <212> DNA  
 <213> Homo sapien

<400> 77  
 ctggagtgcc ttgggtgttc aagccctgc aggaagcaga atgcaccttc tgaggcacct 60  
 ccagctgccc cggcggggga tgcgaggctc ggagcaccct tgcccggctg tgattgtgc 120  
 caggcactgt tcatctcagc tttctgtcc ctttgtccc ggcaagcgt tctgtgaaa 180  
 gttcatatct ggagcctgat gtcttaacga ataaaggctc catgctccac ccgaaaaaaa 240  
 aaaaaaaa 248

<210> 78  
 <211> 201  
 <212> DNA  
 <213> Homo sapien

<400> 78  
 actagtccag tgtggtggaa ttccattgtg ttgggcccac cacaatggct acctttaaca 60  
 tcacccagac ccgcccctgc ccgtgcccac cgctgctgct aacgacagta tgatgcttac 120  
 tctgtactc ggaaactatt tttatgtaat taatgtatgc tttcttggtt ataaatgcct 180  
 gatttaaaaa aaaaaaaaaa a 201

<210> 79  
<211> 552  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(552)  
<223> n = A,T,C or G

<400> 79  
tccttttgtt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg 60  
tttaggcagt gctagtaatt tctcgtaat gattctgtta ttactttcct attctttatt 120  
cctctttctt ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag 180  
tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt 240  
atgcaagtta gtaattactc aggggttaact aaattacttt aatatgctgt tgaacctact 300  
ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga 360  
taatattcta tgttctaaaa gttgggctat acataaanta tnaagaaata tggaatttta 420  
ttcccaggaa tatgggggttc atttatgaat antaccggg anagaagttt tgantnaaac 480  
cngtttttgg taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa 540  
aaaaaaaaaa aa 552

<210> 80  
<211> 476  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(476)  
<223> n = A,T,C or G

<400> 80  
acagggattt gagatgctaa ggccccagag atcgtttgat ccaacctctt tattttcaga 60  
ggggaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct 120  
cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt 180  
gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta 240  
aggttaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatac 300  
tcttctaagt cctcttcag cctcactttg agtcctcctt gggggttgat aggaantntc 360  
tcttggtttt ctcaataaaa tctctatcca tctcatgttt aatttggtag gcntaaaaat 420  
gctgaaaaaa ttaaaatgtt ctggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa 476

<210> 81  
<211> 232  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(232)  
<223> n = A,T,C or G

<400> 81  
tttttttttg tatgcctcn ctgtgngtt attgttgctg ccacctgga ggagcccagt 60  
ttctttctgta tctttctttt ctgggggatc ttctggctc tgccctcca tccccagcct 120  
ctcatcccca tcttgcaatt ttgctagggt tggaggcgt ttctggtag cccctcagag 180  
actcagtcag cggaataag tcctaggggt ggggggtgtg gcaagccggc ct 232

<210> 82  
 <211> 383  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (383)  
 <223> n = A,T,C or G

<400> 82  
 aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc 60  
 agtaccagta ccaataacat gccagtcca gtgccagcac cagtgggtggc ttcagtgtg 120  
 gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggg ggagctgggt 180  
 ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtggat tttagatatt 240  
 gttaatcctg ccagtctttc tcttcaagcc aggtgtgcat ctcagaaacc tactcaaac 300  
 agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg 360  
 ccatttcaaa aaaaaaaaaa aaa 383

<210> 83  
 <211> 494  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (494)  
 <223> n = A,T,C or G

<400> 83  
 accgaattgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca 60  
 gggagatcga gtctatacgc tgaagaaatt tgaccgatg ggacaacaga cctgctcagc 120  
 ccatectgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa 180  
 acgettcaag gtgctcatga ccagcaacc gcgccctgtc ctctgagggt ccttaaaactg 240  
 atgtcttttc tgccacctgt taccctcctg agactcctga accaaaactct tcggactgtg 300  
 agccctgatg cctttttgcc agccatactc tttggcntcc agtctctcgt ggcgattgat 360  
 tatgcttggtg tgaggcaatc atggtggcat caccatnaa gggaacacat ttganttttt 420  
 tttncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactctta 480  
 aaaaaaaaaa aaaa 494

<210> 84  
 <211> 380  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (380)  
 <223> n = A,T,C or G

<400> 84  
 gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca 60  
 agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattccccag 120  
 gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggtctctgtg 180  
 gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgcaa ctggctgggtg 240  
 gtgctgctcc tcgtcatctt cctgctcgtg gccaacatcc tgctggtcac ttgctcattg 300  
 ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360  
 agcgttnccg cctcatccgg 380

<210> 85  
 <211> 481  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(481)  
 <223> n = A,T,C or G

<400> 85  
 gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc 60  
 tnccatcgctc atactgtagg tttgccacca cctcctgcat cttggggcgg ctaatatoca 120  
 ggaaactctc aatcaagtc aacgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180  
 tgtgaaagga tctccagaag gagtgctcga tcttccccac actttttagt actttattga 240  
 gtcgattctg catgtccagc aggaggttgt accagctctc tgacagttag gtcaccagcc 300  
 ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360  
 ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggngaa 420  
 aaagaacacc tcttggaagt gctngccgct cctcgtcctt tgggggnggc gcntnccttt 480  
 t 481

<210> 86  
 <211> 472  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(472)  
 <223> n = A,T,C or G

<400> 86  
 aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt 60  
 acttggaataa gcaacttnaa gcctggacac tgggtattaaa attcacaata tgcaacactt 120  
 taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg 180  
 ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga 240  
 cacaagtccg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt 300  
 catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg 360  
 atatntgagc ggaagantag cttttctact tcaccagaca caactccttt catattggga 420  
 tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472

<210> 87  
 <211> 413  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(413)  
 <223> n = A,T,C or G

<400> 87  
 agaaaccagt atctctnaaa acaacctctc ataccttggt gacctaatTT tgtgtgcgtg 60  
 tgtgtgtgcg cgcataattat atagacaggc acatcttttt tacttttTgt aaagcttatg 120  
 cctctttTgt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct 180  
 ttgtcttctg tgtaaatggg actagagaaa acacctatnt tatgagtcaa tctagtTngt 240  
 tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg 300



```

ggggacaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aattncataa 360
acagaaattg ggtngtatat tgaaanannng catcattnaa acgttttttt ttt 413

```

```

<210> 88
<211> 448
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(448)
<223> n = A,T,C or G

```

```

<400> 88
cgcagcgggt cctctctatc tagctccagc ctctcgectg ccccaactcc cgcgtccgc 60
gtcctagccn accatggccg ggccctgctg cgcctcgctg cctctgctgg ccatcctggc 120
cgtggccctg gccgtgagcc ccgcgcccg ctcagtcctc ggcaagccgc cgcgcctggt 180
gggaggccca tggacccgc gtggaagaag aaggtgtgct gcgtgcactg gactttgccc 240
tcggcnanta caacaaaccc gcaacnactt ttaccnagcn cgcgtgcag gttgtgccgc 300
cccaancaaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng 360
tttaccagaa ccnagccaat tngaacaatt nccctccat aacagccct tttaaaaagg 420
gaancantcc tgntcttttc caaat ttt 448

```

```

<210> 89
<211> 463
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(463)
<223> n = A,T,C or G

```

```

<400> 89
gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca 60
gtagtgtatc tgccaaagt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc 120
agaggtctag gtctgcatat cagcagacag ttgtccgtg tattttgtag ccttgaagtt 180
ctcagtgaca agttntttct gatgcgaagt tctnattcca gtgttttagt cctttgcac 240
tttnatgttn agacttgccct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg 300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn 360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn 420
aattcnnana anttcagntn tcatacaaca naacngganc ccc 463

```

```

<210> 90
<211> 400
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(400)
<223> n = A,T,C or G

```

```

<400> 90
agggattgaa ggtctnttnt actgtcggac tgttcancca ccaactctac aagttgctgt 60
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaaciaat 120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctcttccact 180
tcctttgtta agacttcac 240

```

```

cgttctctaa caatgtcctc tccttgaagt atttggtga acaacccacc tnaagtccct    300
ttgtgcatcc attttaaata tacttaatag ggcattggtg cactagggtta aattctgcaa    360
gagtcacctg tctgcaaaag ttgcgttagt atatctgcca    400

```

```

<210> 91
<211> 480
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (480)
<223> n = A,T,C or G

```

```

<400> 91
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact    60
ggctctacccc acatgggagc agcatgccgt agntatataa ggctattccc tgagtcagac    120
atgcctcttt gactaccgtg tgccagtgtt ggtgattctc acacacctcc nnccgctctt    180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaaat tcacccacga    240
gacacttgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt    300
tgtcaatact aaccgctggg ttgacctcca tcacatttgt gatctgtagc tctggataca    360
tctctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctgtt    420
ngatcaggtt cccatttccc agtcggaatg ttcacatggc atatnttact tcccacaaaa    480

```

```

<210> 92
<211> 477
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (477)
<223> n = A,T,C or G

```

```

<400> 92
atacagccca natcccacca cgaagatgcy cttgttgact gagaacctga tgcggtcact    60
ggctccgctg tagccccagc gactctccac ctgctggaag cgggttgatgc tgcaactcctt    120
cccacgcagg cagcagcggg gccgggtcaat gaactccact cgtggcttgg gggtgacggt    180
taantgcagg aagaggctga ccacctcgcy gtccaccagg atgcccagct gtgcgggacc    240
tgacgcgaaa ctctctgatg gtcatgagcy ggaagcgaat gangcccagg gccttgccca    300
gaaccttcgy cctgttctct ggcgtcacct gcagctgctg ccgctnacac tcggcctcgg    360
accagcggac aaacggcgtt gaacagccgc acctcacgga tgcccantgt gtcgcgtccc    420
aggaacggcn ccagcgtgtc cagggtcaatg tcgggtgaanc ctccgcgggt aatggcg    477

```

```

<210> 93
<211> 377
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (377)
<223> n = A,T,C or G

```

```

<400> 93
gaacggctgg accttgctc gcattgtgct gctggcagga ataccttggc aagcagctcc    60
agtccgagca gcccagacc cctgcccgc gaagctaagc ctgcctctgg ccttcccctc    120
cgctcaatg cagaaccant agtgggagca ctgtgttagt agttaagagt gaacactgtg    180

```

```

tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaata ttccaaacaa 240
caacaacaaa ataacatgtt tgctgttna gttgtataaa agtangtgat tctgtatnta 300
aagaaaatat tactgttaca tatactgctt gcaantttctg tatttattgg tncctctggaa 360
ataaatatat tattaata 377

```

```

<210> 94
<211> 495
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(495)
<223> n = A,T,C or G

```

```

<400> 94
ccctttgagg gggttagggc cagttcccag tggagaagaa aggccaggag aantgcgtgc 60
cgagctgang cagatttccc acagtgaccc cagagccctg ggctatagtc tctgaccct 120
ccaaggaaag accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg 180
gaaggcccca ttccggggct gttcccagag gaggaaggga aggggctctg tgtgcccccc 240
acgaggaana ggccctgant cctgggatca nacaccctt cactgtatc cccacacaaa 300
tgcaagctca ccaaggtccc ctctcagtc ctccctaca ccctgaacgg nacttgccc 360
acaccaccc agancancca cccgccatgg ggaatgtnt caaggaatcg cngggcaacg 420
tggaactctng tcccnnaagg gggcagaatc tccaatagan gganngaacc cttgctnana 480
aaaaaaaaana aaaaa 495

```

```

<210> 95
<211> 472
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

```

```

<400> 95
ggttacttgg ttctattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60
cctctggaag ccttgcgcag agcggacttt gtaattgttg gagaataact gctgaatttt 120
tagctgtttt gaggttgatc gcaccactgc accacaactc aatatgaaa ctatttnact 180
tatttattat ctgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt 240
atgatgaaaa gcaatagata tatattcttt tattatgttn aattatgatt gccattatta 300
atcggaacaaa tgtggagtgt atgttctttt cacagtaata tatgcctttt gtaacttcac 360
ttggttattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata 420
tttanttcan taatttcttt cctgttttac gtaattttg aaaagaatgc at 472

```

```

<210> 96
<211> 476
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

```

```

<400> 96
ctgaagcatt ttttcaaact tntctacttt tgcattgat acctgtagta agttgacaat 60

```

```

gtggtgaaat ttcaaaatta tatgtaactt ctactagttt tactttctcc cccaagtctt      120
ttttaactca tgatttttac acacacaatc cagaacttat tatatagcct ctaagtcttt      180
attcttcaca gtatgatgat aaagagtcct ccagtgtctt gngcanaatg ttctagntat      240
agctggatac atacngtggg agttctataa actcatacct cagtgggact naaccaaaat      300
tgtgttagtc tcaattccta ccacactgag ggagcctccc aaatcactat attcttatct      360
gcaggctact ctccagaaaa acngacaggg caggcttgca tgaaaaagtn acatctgcgt      420
tacaaagtct atcttctcca nangtctgtt aaggaacaat ttaatcttct agcttt      476

```

&lt;210&gt; 97

&lt;211&gt; 479

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; {1}...{479}

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 97

```

actctttcta atgctgatat gatcttgagt ataagaatgc atatgtcact agaatggata      60
aaataatgct gcaaacttaa tgttcttatg caaaatggaa cgctaataaa acacagctta      120
caatcgcaaa tcaaaactca caagtgtctc tctgttgtag atttagtgta ataagactta      180
gattgtgtct cttcggatat gattgtttct canatcttgg gcaatnttcc ttagtcaaat      240
caggctacta gaattctggt attggatatn tgagagcatg aaatttttaa naatacactt      300
gtgattatna aattaatcac aaatttctact tatacctgct atcagcagct agaaaaacat      360
ntnnttttta natcaaagta ttttgtgttt ggaantgttn aaatgaaatc tgaatgtggg      420
ttcnatctta ttttttcccn gacnactant tnttttttta gggncatttc tganccatc      479

```

&lt;210&gt; 98

&lt;211&gt; 461

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 98

```

agtgacttgt cctccaacaa aacccttga tcaagtttgt ggcactgaca atcagaccta      60
tgctagtctc tgcctcttat tcgctactaa atgcagactg gaggggacca aaaaggggca      120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga      180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatctctca tgcagcttta      240
tgaagccact ctgaacacgc tggttatcta gatgagaaca gagaaataaa gtcagaaaat      300
ttacctggag aaaagaggct ttggctgggg accatcccat tgaaccttct cttaggact      360
ttaagaaaaa ctaccacatg ttgtgtatcc tgggtgccggc cgtttatgaa ctgaccaccc      420
tttggataaa tcttgacgct cctgaacttg ctctcttgcg a      461

```

&lt;210&gt; 99

&lt;211&gt; 171

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 99

```

gtggcgcgcg gcagggtgtt cctcgtagcg caggggcccc tcccttcccc aggcgtccct      60
cggcgcctct gcgggcccga ggaggagcgg ctggcggttg gggggagtgt gaccacccct      120
cggtgagaaa agccttctct agcgatctga gaggcgtgcc ttgggggtac c      171

```

&lt;210&gt; 100

&lt;211&gt; 269

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 100

cgccgcgaag	tgcaactcca	gctggggccg	tgccgacgaa	gattctgcc	gcagttggtc	60
cgactgcgac	gacggcgccg	gcgacagtcg	caggtgcagc	gcgggcgcct	gggtcttgc	120
aaggctgagc	tgacgccgca	gaggtcgtgt	cacgtccac	gacctgacg	ccgtcgggga	180
cagccggaac	agagcccgg	gaagcgggag	gcctcgggga	gcccctcggg	aagggcgcc	240
cgagagatac	gcaggtgcag	gtggccgcc				269

&lt;210&gt; 101

&lt;211&gt; 405

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 101

tttttttttt	ttttggaatc	tactgcgagc	acagcaggtc	agcaacaagt	ttattttgca	60
gctagcaagg	taacagggtg	gggcatggtt	acatgttcag	gtcaacttcc	ttgtcgtgg	120
ttgattggtt	tgtctttatg	ggggcggggt	ggggtagggg	aaacgaagca	aataacatgg	180
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tgaccgtcat	tttcttgaca	tcaatgttat	tagaagtcag	gatattcttt	agagagtcca	300
ctgttctgga	gggagattag	ggtttcttgc	caaatccaac	aaaatccact	gaaaaagttg	360
gatgatcagt	acgaataccg	aggcatattc	tcatatcgtt	ggcca		405

&lt;210&gt; 102

&lt;211&gt; 470

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 102

tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	60
ggcacttaat	ccatttttat	ttcaaaatgt	ctacaaattt	aatcccat	tacggttatt	120
tcaaaatcta	aattattcaa	attagccaaa	tccttaccaa	ataataccca	aaaatcaaaa	180
atatacttct	ttcagcaaac	ttgttacata	aattaaaaaa	atatatacgg	ctgggtgttt	240
caaagtacaa	ttatcttaac	actgcaaaaca	ttttaaggaa	ctaaaaataa	aaaaaacact	300
ccgcaaagggt	taaagggaac	aacaaattct	tttacaacac	cattataaaa	atcatatctc	360
aaatcttagg	ggaatatata	cttcacacgg	gatcttaact	tttactcact	ttgtttattt	420
ttttaaacca	ttgtttgggc	ccaacacaat	ggaatcccc	ctggactagt		470

&lt;210&gt; 103

&lt;211&gt; 581

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 103

tttttttttt	ttttttttga	ccccctctt	ataaaaaaca	agttaccatt	ttattttact	60
tacacatatt	tattttataa	ttggtattag	atattcaaaa	ggcagctttt	aaaatcaaac	120
taaatggaaa	ctgccttaga	tacataattc	ttaggaatta	gcttaaaatc	tgccctaaagt	180
gaaaatcttc	tctagctctt	ttgactgtaa	atttttgact	cttgtaaaac	atccaaattc	240
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gcttctctag	cctcatttcc	tagctcttat	ctactattag	taagtggctt	ttttcctaaa	360
agggaaaaaca	ggaagagaaa	tgccacacaa	aacaaacatt	ttatattcat	attttctacct	420
acgttaataa	aatagcattt	tgtgaagcca	gctcaaaaga	aggcttagat	ccttttatgt	480
ccattttagt	cactaaacga	tatcaaagtg	ccagaatgca	aaaggtttgt	gaacatttat	540
tcaaaagcta	atataagata	tttcacatac	tcattctttc	g		581

&lt;210&gt; 104

&lt;211&gt; 578

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 104

tttttttttt	tttttttttt	tttttctctt	cttttttttt	gaaatgagga	tcgagttttt	60
cactctctag	atagggcatg	aagaaaactc	atctttccag	ctttaaaata	acaatcaa	120
ctcttatgct	atatcatatt	ttaagttaaa	ctaagagtc	actggcttat	cttctcctga	180
aggaaatctg	ttcattcttc	tcattcatat	agttatatca	agtactacct	tgcatattga	240
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caaaactgct	caaattgttt	gttaagttat	ccattataat	tagttggcag	gagctaatac	420
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tgaattcaca	tggtattatt	cctagcccaa	cacaatgg			578

&lt;210&gt; 105

&lt;211&gt; 538

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 105

tttttttttt	tttttcagta	ataatcagaa	caatatttat	ttttatattt	aaaattcata	60
gaaaagtgcc	ttacatttaa	taaaagtgtg	tttctcaaa	tgatcagagg	aattagatat	120
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aagatcatag	agcttgtaag	tgaaaagata	aaatttgacc	tcagaaactc	tgagcattaa	240
aatccacta	ttagcaata	aattactatg	gacttcttgc	tttaattttg	tgatgaatat	300
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agatatgttt	cctttgcaa	tattaaaaaa	ataataatgt	ttactactag	tgaacc	538

&lt;210&gt; 106

&lt;211&gt; 473

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 106

tttttttttt	tttttttagtc	aagtttctat	ttttattata	attaaagtct	tggtcatttc	60
atttattagc	tctgcaactt	acatatttaa	attaaagaaa	cgtttttagac	aactgtacaa	120
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cgccttctc	aaaggcgtg	ccacatttgt	ggctctttgc	acttgtttca	aaa	473

&lt;210&gt; 107

&lt;211&gt; 1621

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 107

cgccatggca	ctgcagggca	tctcggtcat	ggagctgtcc	ggcctggccc	cgggcccggt	60
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cttcgcgcgc	gggtgcatgg	agaaactcca	gctgggccc	gagattctgc	agcgggaaaa	300
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agctggccac	gatatacaact	atttggcttt	gtcaggtgtt	ctctcaaaaa	ttggcagaag	420
tggtgagaat	ccgtatgccc	cgctgaatct	cctggctgac	tttgctggtg	tgggccttat	480
gtgtgcactg	ggcattataa	tggtcttttt	tgaccgcaca	cgcactgaca	agggtcaggt	540

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cattgatgca aatatggtgg aaggaaacagc atattttaagt tcttttctgt ggaaaactca 600
gaaatcgagt ctgtgggaag cacctcgagg acagaacatg ttggatggtg gagcaccttt 660
ctatacgact tacaggacag cagatgggga attcatggct gttggagcaa tagaacccca 720
gttctacgag ctgctgatca aaggacttgg actaaagtct gatgaacttc ccaatcagat 780
gagcatggat gattggccag aaatgaagaa gaagtttgca gatgtatttg caaagaagac 840
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cagccgcgaa gagattttatc agcttaactc agataaaatc attgaaagta ataaggtaaa 1140
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agttattctg ccttccagtt tgcttgatat atttgttgat attaagattc ttgacttata 1440
ttttgaatgg gttctagtga aaaaggaatg atatatctct gaagacatcg atatacattt 1500
atttacactc ttgattctac aatgtagaaa atgaggaaat gccacaaatt gtatggtgat 1560
aaaagtcacg tgaacaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620
a

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&lt;210&gt; 108

&lt;211&gt; 382

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 108

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Met Ala Leu Gln Gly Ile Ser Val Met Glu Leu Ser Gly Leu Ala Pro
1      5      10      15
Gly Pro Phe Cys Ala Met Val Leu Ala Asp Phe Gly Ala Arg Val Val
20     25     30
Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg
35     40     45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
50     55     60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65     70     75     80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85     90     95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
100    105    110
Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115    120    125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130    135    140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
145    150    155    160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165    170    175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180    185    190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195    200    205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg
210    215    220
Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe
225    230    235    240
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro
245    250    255

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<210> 109
<211> 1524
<212> DNA
<213> Homo sapien
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<400> 109

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cagaggaaaa	aaaaaaaaaa	aaaa				1524

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<210> 110
<211> 3410
<212> DNA
<213> Homo sapien
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<400> 110

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ggtgagccgc	ctgctgcggc	accggaaaagc	ccagctcttg	ctggtcaacc	tgctaaccctt	360
tggcctggag	gtgtgttttg	ccgcaggcat	cacctatgtg	ccgcctctgc	tgctggaagt	420
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aaaaaaaaara	aaaaaaaaaa	aaaaaaaaaa	aaaaaaataa	aaaaaaaaaa		3410

&lt;210&gt; 111

&lt;211&gt; 1289

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 111

```

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ccatgcagtg cttcagcttc attaaagacca tgatgatcct cttcaatttg ctcactcttc 180
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tgaagatctt cgggccactg tcgtccagtg ccatgcagtt tgtcaacgtg ggctacttcc 300
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tgttacaatg ttaaaaaaaaa aaaaaaaaaa 1289

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&lt;210&gt; 112

&lt;211&gt; 315

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 112

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Met Val Phe Thr Val Arg Leu Leu His Ile Phe Thr Val Asn Lys Gln
1          5          10          15
Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe
20          25          30
Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala
35          40          45
Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu
50          55          60
Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro
65          70          75          80
Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser
85          90          95
Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys
100         105         110
Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Leu Val Ile Phe
115         120         125
Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe
130         135         140
Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys
145         150         155         160
Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu
165         170         175
Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Leu Arg Gln
180         185         190
Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu

```

195                      200                      205  
 His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr  
 210                      215                      220  
 Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp  
 225                      230                      235                      240  
 Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val  
 245                      250                      255  
 Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg  
 260                      265                      270  
 Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly  
 275                      280                      285  
 Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly  
 290                      295                      300  
 Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp  
 305                      310                      315

<210> 113  
 <211> 553  
 <212> PRT  
 <213> Homo sapien

<400> 113  
 Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala  
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 20                      25                      30  
 Ala Ala Gly Ile Thr Tyr Val Pro Leu Leu Leu Glu Val Gly Val  
 35                      40                      45  
 Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly  
 50                      55                      60  
 Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly  
 65                      70                      75                      80  
 Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile  
 85                      90                      95  
 Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu  
 100                      105                      110  
 Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly  
 115                      120                      125  
 Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu  
 130                      135                      140  
 Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala  
 145                      150                      155                      160  
 Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr  
 165                      170                      175  
 Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu  
 180                      185                      190  
 Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu  
 195                      200                      205  
 Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly  
 210                      215                      220  
 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His  
 225                      230                      235                      240  
 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu  
 245                      250                      255  
 Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg  
 260                      265                      270  
 Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe  
 275                      280                      285

Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val  
 290 295 300  
 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly  
 305 310 315 320  
 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu  
 325 330 335  
 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg  
 340 345 350  
 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala  
 355 360 365  
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu  
 370 375 380  
 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala  
 385 390 395 400  
 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly  
 405 410 415  
 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu  
 420 425 430  
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala  
 435 440 445  
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser  
 450 455 460  
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala  
 465 470 475 480  
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp  
 485 490 495  
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser  
 500 505 510  
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala  
 515 520 525  
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp  
 530 535 540  
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
 545 550

&lt;210&gt; 114

&lt;211&gt; 241

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 114

Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu  
 1 5 10 15  
 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val  
 20 25 30  
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser  
 35 40 45  
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly  
 50 55 60  
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr  
 65 70 75 80  
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile  
 85 90 95  
 Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr  
 100 105 110  
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys  
 115 120 125  
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met

130		135		140
Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp				
145		150		155
Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn				160
	165		170	175
Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala				
	180		185	190
His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile				
	195		200	205
Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly				
	210		215	220
Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu				
225		230		235
Gln				240

<210> 115  
 <211> 366  
 <212> DNA  
 <213> Homo sapien

<400> 115	
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catttcaactg tgatgtatat tgtgttgcaa aaaaaaaaaa gtgtctttgt ttaaaattac	120
ttggtttggt aatccatctt gctttttccc cattggaact agtcattaac ccatctctga	180
actggtagaa aaacatctga agagctagtc tatcagcadc tgacagggtga attggatggt	240
tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt	300
tctctacatg cataacaaac cctgtccaa tctgtcacat aaaagtctgt gacttgaagt	360
ttagtc	366

<210> 116  
 <211> 282  
 <212> DNA  
 <213> Homo sapien

<220>	
<221> misc_feature	
<222> (1)...(282)	
<223> n = A,T,C or G	
<400> 116	
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gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa	120
agactttact attttcatat tttaagacac atgatttadc ctatttttagt aacctgggtc	180
atacggttaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt	240
tcaatctnga actatctana tcacagacat ttctattcct tt	282

<210> 117  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(305)  
 <223> n = A,T,C or G

<400> 117

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aataaggcaa aatatatgaa acaacagggtc tcgagatatt ggaaatcagt caatgaagga      180
tactgatccc tgatcactgt cctaatagcag gatgtgggaa acagatgagg tcacctctgt      240
gactgcccca gcttactgcc thtagagagt ttctangctg cagttcagac agggagaaat      300
tgggt                                           305

```

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<210> 118
<211> 71
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(71)
<223> n = A,T,C or G

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```

<400> 118
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aantcctggg t                                           71

```

```

<210> 119
<211> 212
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(212)
<223> n = A,T,C or G

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<400> 119
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gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac      120
agtaagctgg cccttctaataaaaagaaaat tgaaagggtt ctcactaanc ggaattaant      180
aatggantca aganactccc aggcctcagc gt                                           212

```

```

<210> 120
<211> 90
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(90)
<223> n = A,T,C or G

```

```

<400> 120
actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tgggtcttgcc      60
ctccgccggc gcagaacatg ctggggtggt                                           90

```

```

<210> 121
<211> 218
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```

&lt;222&gt; (1)...(218)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 121

tgtancgtga anacgacaga nagggttgtc aaaaatggag aanccttgaa gtcattttga	60
gaataagatt tgctaaaaga tttggggcta aaacatgggtt attgggagac atttctgaag	120
atatncangt aaattangga atgaattcat gggtcttttg ggaattcctt tacgatngcc	180
agcatanact tcatgtgggg atancagcta cccttgta	218

&lt;210&gt; 122

&lt;211&gt; 171

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 122

taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg	60
catttgtagt ctcatggaac aggaagtcgg atggtggggc atcttcagtg ctgcatgagt	120
caccaccccg gcgggggtcat ctgtgccaca ggtccctgtt gacagtgcgg t	171

&lt;210&gt; 123

&lt;211&gt; 76

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(76)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 123

tgtagcgtga agacnacaga atggtgtgtg ctgtgctatc caggaacaca tttattatca	60
ttatcaanta ttgtgt	76

&lt;210&gt; 124

&lt;211&gt; 131

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 124

acctttcccc aaggccaatg tctgtgtgtc taactggccg gctgcaggac agctgcaatt	60
caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg	120
ttaagatttg t	131

&lt;210&gt; 125

&lt;211&gt; 432

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 125

actttatcta ctggctatga aatagatggg ggaattgtgc gttaccaact ataccactgg	60
cttgaaaaag aggtgatagc tcttcagagg acttgtgact tttgctcaga tgctgaagaa	120
ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat	180
ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg	240
ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc	300
catgggtggg gtcttgcac tgtaagaatg gaattgattt tgcttttgca agaattctcag	360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaacctc agtgcctctc	420
ctctttgctt gt	432

<210> 126  
<211> 112  
<212> DNA  
<213> Homo sapien

<400> 126  
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat 60  
agtaagaatg atatttcccc ccagggatca ccaaatttt ataaaaattt gt 112

<210> 127  
<211> 54  
<212> DNA  
<213> Homo sapien

<400> 127  
accacgaaac cacaacaag atggaagcat caatccactt gccaaagcaca gcag 54

<210> 128  
<211> 323  
<212> DNA  
<213> Homo sapien

<400> 128  
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctccct ctaccagctc 60  
acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgtca 120  
ttctctctga agtctaggtt acccattttg gggaccatt ataggcaata aacacagttc 180  
ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcccttt tcttagcctt 240  
ttcctgcaaa aggctcactc agtcccttgc ttgtcagtg gactgggctc cccagggcct 300  
aggctgcctt cttttccatg tcc 323

<210> 129  
<211> 192  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)... (192)  
<223> n = A,T,C or G

<400> 129  
acatacatgt gtgtatattt ttaaataatca cttttgtatc actctgactt tttagcatac 60  
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc 120  
tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg 180  
gataaacaaa gt 192

<210> 130  
<211> 362  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)... (362)  
<223> n = A,T,C or G

<400> 130  
ccctttttta tggaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca 60



```
tataatgacg caacaaaaag gtgctgttta gtctatggt tcagtttatg cccctgacaa 120
gtttccattg tgttttgccg atcttctggc taatcggtgt atcctccatg ttattagtaa 180
ttctgtattc cattttgtta acgcttggtg gatgtaacct gctangaggc taactttata 240
cttatttaaa agctcttatt ttgtggcat taaaatggca atttatgtgc agcactttat 300
tgcagcagga agcacgtgtg ggttggttgt aaagctcttt gctaattcta aaaagtaatg 360
gg 362
```

&lt;210&gt; 131

&lt;211&gt; 332

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(332)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 131

```
ctttttgaaa gatcgtgtcc actcctgtgg acatcttgtt ttaatggagt tccccatgca 60
gtangactgg tatggttgca gctgtccaga taaaaacatt tgaagagctc caaaatgaga 120
gtttctccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc 180
ttctgaacta gattaaggca gcttgtaaat ctgatgtgat ttggtttatt atccaactaa 240
cttccatctg ttatcactgg agaaagccca gactccccan gacnggtacg gattgtgggc 300
atanaaggat tgggtgaagc tggcgttgtg gt 332
```

&lt;210&gt; 132

&lt;211&gt; 322

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(322)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 132

```
acttttgcca ttttgtatat ataaacaatc ttgggacatt ctctgaaaa ctaggtgtcc 60
agtggctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat 120
ctcaaattcc caaacagggg ctctgtggga aaaatgaggg aggaccttg tatctcgggt 180
tttagcaagt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttg 240
ggatgcttct aaaaaaaact ttggtagaga aaataggaat gctnaatcct aggaagcct 300
gtaacaatct acaattggtc ca 322
```

&lt;210&gt; 133

&lt;211&gt; 278

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(278)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 133

```
acaagccttc acaagtttaa ctaaattggg attaatcttt ctgtanttat ctgcataatt 60
cttgtttttc tttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta 120
ctatttaaaa aaaatcacia atctttccct ttaagctatg ttnaattcaa actattcctg 180
ctattcctgt ttgtcaaag aaattatatt ttcaaaaata tgnatatttg tttgatgggt 240
```

cccacgaaac actaataaaa accacagaga ccagcctg

278

<210> 134

<211> 121

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(121)

<223> n = A,T,C or G

<400> 134

gtttanaaaa cttgttttagc tccatagagg aaagaatggt aaactttgta ttttaaaaca 60  
tgattctctg aggttaaact tggttttcaa atgttatatt tacttgatt ttgcttttgg 120  
t 121

<210> 135

<211> 350

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(350)

<223> n = A,T,C or G

<400> 135

acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctataacc 60  
atancaagtgt gtgactgggt aagcgtgcga caaagggtcag ctggcacatt acttggtgtgc 120  
aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtagtcca 180  
gggtgcccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgct 240  
ccacctcaat caagccctgg gccatgctac ctgcaattgg ctgaacaaac gtttgctgag 300  
ttcccaagga tgcaaagcct ggtgctcaac tctggggcg tcaactcagt 350

<210> 136

<211> 399

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(399)

<223> n = A,T,C or G

<400> 136

tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga ggccagggtt 60  
gctgtgattg tatccgaata ntccctgtga gaaaagataa tgagatgacg tgagcagcct 120  
gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga 180  
cctggcggcc agccagccag ccacaggtgg gcttcttct tttgtggtga caacnccaag 240  
aaaactgcag aggccagggt tcaggtgtna gtgggtangt gaccataaaa caccagggtgc 300  
tcccaggaac ccgggcaaag gccatcccca cctacagcca gcatgcccac tggcgtgatg 360  
ggtgcagang gatgaagcag ccagntgttc tgctgtggt 399

<210> 137

<211> 165

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(165)  
 <223> n = A,T,C or G

<400> 137  
 actggtgtgg tnggggtga tgctggtgg anaagttgan gtgacttcan gatggtgtgt 60  
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120  
 ttggctgggc ccactggtgg tcaactgtcat tgggtggggtt cctgt 165

<210> 138  
 <211> 338  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(338)  
 <223> n = A,T,C or G

<400> 138  
 actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc 60  
 ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa 120  
 tgctgggcag tctcccatgc ctccacagt gaaagggctt gagaaaaatc acatccaatg 180  
 tcatgtgttt ccagccacac caaaagggtgc ttgggggtgga gggctggggg catananggt 240  
 cangcctcag gaagcctcaa gtccattca gctttgccac tgtacattcc ccatntttaa 300  
 aaaaactgat gccttttttt tttttttttg taaaattc 338

<210> 139  
 <211> 382  
 <212> DNA  
 <213> Homo sapien

<400> 139  
 gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa 60  
 gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccgaa gtgaaggaga 120  
 attcaaacag acctcgcat tcttggtgtg agcctggctg gctcaccgcc tatcatctgc 180  
 atttgctta ctcaggtgct accgactct ggccctgat gtctgtagtt tcacaggatg 240  
 ccttatttgt cttctacacc ccacagggcc cctacttct tcggatgtgt ttttaataat 300  
 gtcagctatg tgcccatcc tccttcatgc cctccctccc tttcctacca ctgctgagtg 360  
 gcctggaact tgtttaaagt gt 382

<210> 140  
 <211> 200  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(200)  
 <223> n = A,T,C or G

<400> 140  
 accaaanctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat 60  
 acttttcatt taacancttt tgttaagtgt caggctgcac tttgctccat anaattattg 120  
 ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt 180  
 atattcagca taaaggagaa 200

<210> 141  
<211> 335  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(335)  
<223> n = A,T,C or G

<400> 141  
actttatttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg 60  
gggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc agggtttgtt 120  
atgcatgtag agaaccctaaa ctaattttatt aaacaggata gaaacaggct gtctgggtga 180  
aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg 240  
tttttctacc agttcagaga tnggttaatg actantttcca atgggggaaaa agcaagatgg 300  
attcacaac caagtaattt taaacaaaga cactt 335

<210> 142  
<211> 459  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(459)  
<223> n = A,T,C or G

<400> 142  
accagggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta 60  
gggttggtta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat 120  
ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca 180  
cacatggtcc aacaacactc aaataataaa tcaaataatna tcagatgtta aagattggtc 240  
ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca 300  
tcaacacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga 360  
agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct 420  
cagcanggggt gggaggaacc agctcaacct tggcgctant 459

<210> 143  
<211> 140  
<212> DNA  
<213> Homo sapien

<400> 143  
acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg 60  
aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag 120  
accatccgac ttccctgtgt 140

<210> 144  
<211> 164  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(164)  
<223> n = A,T,C or G

<400> 144  
 acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct 60  
 atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg 120  
 aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt 164

<210> 145  
 <211> 303  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(303)  
 <223> n = A,T,C or G

<400> 145  
 acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa 60  
 actggagggt atttatcccc aattatcccc ttcattaaca tgccctcctc ctcaggctat 120  
 gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca 180  
 gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag 240  
 tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat 300  
 caa 327

<210> 146  
 <211> 327  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(327)  
 <223> n = A,T,C or G

<400> 146  
 actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac 60  
 actggcctgg agtgactcat tgctctggtt ggttgagaga gctcctttgc caacaggcct 120  
 ccaagtcagg gctgggattt gtttccttcc cacattctag caacaatatg ctggccactt 180  
 cctgaacagg gagggtgagg ggagccagca tggaacaagc tgccacttcc taaagtagcc 240  
 agacttgccc ctgggcctgt cacacctact gatgacctc tgtgcctgca ggatggaatg 300  
 taggggtgag ctgtgtgact ctatggt 327

<210> 147  
 <211> 173  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(173)  
 <223> n = A,T,C or G

<400> 147  
 acattgtttt ttgagataa agcattgana gagctctcct taacgtgaca caatggaagg 60  
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120  
 atattcaagc acatatgtta tatattatcc agttccatgt ttatagccta gtt 173

<210> 148

&lt;211&gt; 477

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(477)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 148

acaaccaatt	tatctcatcg	aatttttaac	ccaaactcac	tcactgtgcc	tttctatcct	60
atgggatata	ttatttgatg	ctccatttca	tcacacatat	atgaataata	cactcatact	120
gccctactac	ctgctgcaat	aatcacattc	ccttcctgtc	ctgaccctga	agccattggg	180
gtgggtcctag	tggccatcag	tccangcctg	caccttgagc	ccttgagctc	cattgctcac	240
nccancccac	ctcaccgacc	ccatcctctt	acacagctac	ctccttgctc	tctaacccca	300
tagattatnt	ccaaattcag	tcaattaagt	tactattaac	actctaccgg	acatgtccag	360
caccactggg	aagccttctc	cagccaacac	acacacacac	acacncacac	acacacatat	420
ccaggcacag	gctacctcat	cttcacaatc	acccttttaa	ttaccatgct	atggtgg	477

&lt;210&gt; 149

&lt;211&gt; 207

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 149

acagttgtat	tataatatca	agaaataaac	ttgcaatgag	agcattttaag	aggggaagaac	60
taacgtatnt	tagagagcca	aggaagggtt	ctgtggggag	tgggatgtaa	ggtggggcct	120
gatgataaat	aagagtcagc	caggtaagtg	ggtggtgtgg	tatgggcaca	gtgaagaaca	180
tttcaggcag	aggggaacagc	agtgaaa				207

&lt;210&gt; 150

&lt;211&gt; 111

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(111)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 150

accttgattt	cattgctgct	ctgatggaaa	cccaactatc	taatttagct	aaaacatggg	60
cacttaaatg	tggtcagtgt	ttggacttgt	taactantgg	catctttggg	t	111

&lt;210&gt; 151

&lt;211&gt; 196

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 151

agcgcggcag	gtcatattga	acattccaga	tacctatcat	tactcgatgc	tgttgataac	60
agcaagatgg	ctttgaactc	agggtcacca	ccagctattg	gaccttacta	tgaaaacat	120
ggataccaac	cggaaaaccc	ctatcccga	cagcccactg	tggtccccac	tgtctacgag	180
gtgcatccgg	ctcagt					196

&lt;210&gt; 152

&lt;211&gt; 132

&lt;212&gt; DNA

<213> Homo sapien

<400> 152

acagcacttt cacatgtaag aaggagaaa ttcctaaatg taggagaaag ataacagAAC	60
cttccccttt tcatctagtgt gtggaaacct gatgctttat gttgacagga atagaaccag	120
gagggagtgt gt	132

<210> 153

<211> 285

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (285)

<223> n = A,T,C or G

<400> 153

acaanaccca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag	60
cttctgctct tatgtcctca tctgacaact ctttaccatt tttatcctcg ctcagcagga	120
gcacatcaat aaagtccaaa gtcttggaact tggccttggc ttggaggaag tcatcaacac	180
cctggctagt gaggtgctgg cgccgtcctt ggatgacggc atctgtgaag tcgtgcacca	240
gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt	285

<210> 154

<211> 333

<212> DNA

<213> Homo sapien

<400> 154

accacagtcc tgttggggcca gggcttcatg accctttctg tgaaaagcca tattatcacc	60
accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac	120
cctaagccgg ttacacagct aactcccact ggccctgatt tgtgaaattg ctgctgcctg	180
attggcacag gagtccaagg tgttcagctc ccctcctcgg tggaacgaga ctctgatttg	240
agtttcacaa attctcgggc cacctcgtca ttgctcctct gaaataaaat ccggagaatg	300
gtcaggcctg tctcatccat atggatcttc cgg	333

<210> 155

<211> 308

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (308)

<223> n = A,T,C or G

<400> 155

actggaata ataaaaccca catcacagtgt ttgtgtcaaa gatcatcagg gcatggatgg	60
gaaagtgttt tgggaactgt aaagtgccta acacatgac gatgattttt gttataatat	120
ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tgggccccag cccagcccc	180
atcacagctc actgctctgt tcatccaggc ccagcatgta gtggctgatt cttcttggt	240
gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcattgctg	300
gccctggt	308

<210> 156

<211> 295

<212> DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 156

accttgctcg	gtgcttggaa	catattagga	actcaaaata	tgagatgata	acagtgccta	60
ttattgatta	ctgagagaac	tgtagacat	ttagttgaag	attttctaca	caggaaactga	120
gaataggaga	ttatgtttgg	cctcatatt	ctctcctatc	ctccttgcc	cattctatgt	180
ctaatatatt	ctcaatcaaa	taaggttagc	ataatcagga	aatcgaccaa	ataccaatat	240
aaaaccagat	gtctatcctt	aagattttca	aatagaaaac	aaattaacag	actat	295

&lt;210&gt; 157

&lt;211&gt; 126

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 157

acaagtttaa	atagtgtgt	cactgtgcat	gtgctgaaat	gtgaaatcca	ccacatttct	60
gaagagcaaa	acaaattctg	tcatgtaac	tctatcttgg	gtcgtgggta	tatctgtccc	120
cttagt						126

&lt;210&gt; 158

&lt;211&gt; 442

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(442)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 158

accactggt	cttggaaca	ccatcctta	atacgatgat	ttttctgtcg	tgtgaaaatg	60
aanccagcag	gctgccctta	gtcagtcctt	ccttccagag	aaaaagagat	ttgagaaagt	120
gcctgggtaa	ttcaccatta	atttctctcc	ccaaactctc	tgagtcttcc	cttaatatatt	180
ctgggtgttc	tgaccaaaagc	aggatcatggt	ttgttgagca	tttgggatcc	cagtgaagta	240
natgtttgta	gccttgcata	cttagccctt	cccacgcaca	aacggagtgg	cagagtgggtg	300
ccaaccctgt	tttcccagtc	cacgtagaca	gattcacagt	gcggaattct	ggaagctgga	360
nacagacggg	ctctttgcag	agccgggact	ctgagangga	catgagggcc	tctgcctctg	420
tgttcattct	ctgatgtcct	gt				442

&lt;210&gt; 159

&lt;211&gt; 498

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(498)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 159

acttccaggt	aacgttggtg	tttccgttga	gcctgaactg	atgggtgacg	ttgtaggttc	60
tccaacaaga	actgaggttg	cagagcgggt	aggaagagt	gctgttccag	ttgcacctgg	120
gctgctgtgg	actgttggtg	attcctcact	acggcccaag	gttgtggaac	tggcanaaag	180
gtgtgttggt	gganttgagc	tcgggcggct	gtggtaggtt	gtgggctctt	caacaggggc	240
tgctgtgggtg	ccgggangtg	aangtgttgt	gtcacttgag	cttggccagc	tctggaaagt	300
antanattct	tcctgaaggc	cagcgcttgt	ggagctggca	ngggtcantg	ttgtgtgtaa	360
cgaaccagtg	ctgctgtggg	tgggtgtana	tcctccacaa	agcctgaagt	tatggtgtcn	420
tcaggtaana	atgtgggttc	agtgtccctg	ggcngctgtg	gaaggttgta	nattgtcacc	480



aagggaataa gctgtggt

498

&lt;210&gt; 160

&lt;211&gt; 380

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(380)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 160

acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac	60
agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct	120
ggagcatggc atagaggaag ctganaaatg tggggtctga ggaagccatt tgagtctggc	180
cactagacat ctcacagcc acttgtgtga agagatgccc catgacccca gatgcctctc	240
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg	300
gagaaaaatg gcagtttgac cgaacctggt cacaacggta gaggctgatt tctaacgaaa	360
ctgtagaat gaagcctgga	380

&lt;210&gt; 161

&lt;211&gt; 114

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 161

actccacatc ccctctgagc aggcgggtgt cgttcaaggt gtatttggcc ttgcctgtca	60
cactgtccac tggccctta tccacttggg gcttaatccc tcgaaagagc atgt	114

&lt;210&gt; 162

&lt;211&gt; 177

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 162

actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa	60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt	120
tggtgatata taacttgga ataaccagc ctggtgatac ataaaactac tcaactgt	177

&lt;210&gt; 163

&lt;211&gt; 137

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(137)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 163

catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtagc	60
canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt	120
catcagcggc atgatgt	137

&lt;210&gt; 164

&lt;211&gt; 469

&lt;212&gt; DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(469)

<223> n = A,T,C or G

<400> 164

cttatcacia	tgaatgttct	cctgggcagc	gttgtgatct	ttgccacett	cgtgacttta	60
tgcaatgcat	catgctat	ttt caca	ctaata	gagggagttc	caggagattc	aaccaggaaa 120
tgcatggatc	tcaaaggaaa	caaacaccca	ataaactcgg	agtggcagac	tgacaactgt	180
gagacatgca	cttgctacga	aacagaaatt	tcatgttgca	cccttgtttc	tacacctgtg	240
ggttatgaca	aagacaactg	caaagaatc	ttcaagaagg	aggactgcaa	gtatatcgtg	300
gtggagaaga	aggacccaaa	aaagacctgt	tctgtcagtg	aatggataat	ctaattgtgt	360
tctagtaggc	acagggctcc	caggccaggc	ctcattctcc	tctggcctct	aatagtcaat	420
gattgtgtag	ccatgcctat	cagtaaaaag	atntttgagc	aaacactttt		469

<210> 165

<211> 195

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(195)

<223> n = A,T,C or G

<400> 165

acagtttttt	atanatatcg	acattgcccg	cacttgtgtt	cagtttcata	aagctgggtg	60
atccgctgtc	atccactatt	ccttggttag	agtaaaaatt	attcttatag	cccattgtccc	120
tgcagggccc	ccgcccgtag	ttctcggtcc	agtcgtcttg	gcacacaggg	tgccaggact	180
tcctctgaga	tgagt					195

<210> 166

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 166

acatcttagt	agtgtggcac	atcagggggc	catcagggtc	acagtcactc	atagcctcgc	60
cgaggtcggg	gtccacacca	ccggtgtagg	tgtgtctaat	cttgggcttg	gcgcccacct	120
ttggagaagg	gatattgctg	acacacatgt	ccacaaagcc	tgtgaactcg	ccaaagaatt	180
tttgagacc	agcctgagca	aggggcggat	gttcagcttc	agctcctcct	tcgtcaggtg	240
gatgccaacc	tcgtctangg	tcggtgggaa	gctgggtgtc	acntcaccta	caacctgggc	300
gangatctta	taaagaggct	ccnagataaa	ctccacgaaa	cttctctggg	agctgctagt	360
nggggccttt	ttggtgaact	ttc				383

<210> 167

<211> 247

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(247)  
 <223> n = A,T,C or G

<400> 167  
 acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtcganat 60  
 tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc 120  
 tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac 180  
 tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac 240  
 tgangtc 247

<210> 168  
 <211> 273  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(273)  
 <223> n = A,T,C or G

<400> 168  
 acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa 60  
 aatccctcan ccttgttctt cactactgtc tatactgana gtgtcatgtt tccacaaagg 120  
 gctgacacct gagcctgnat tttactcat ccttgagaag ccctttccag taggggtgggc 180  
 aattcccaac ttccttgcca caagcttccc aggcctttctc ccctggaaaa ctccagcttg 240  
 agtcccagat acactcatgg gctgccctgg gca 273

<210> 169  
 <211> 431  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(431)  
 <223> n = A,T,C or G

<400> 169  
 acagccttgg cttccccaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc 60  
 agctcagacc aggggtcaaag gatgtgacat caacagtttc tggtttcaga acaggttcta 120  
 ctactgtcaa atgaccccc atacttctc aaaggctgtg gtaagttttg cacaggtgag 180  
 ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccacttgac 240  
 cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tctactgctgg gcaccagctc 300  
 acgcacatca ctgacaaccg ggatggaaaa agaantgcc aactttcatac atccaactgg 360  
 aaagtgatct gatactggat tcttaattac cttcaaaagc ttctgggggc catcagctgc 420  
 tcgaacactg a 431

<210> 170  
 <211> 266  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(266)  
 <223> n = A,T,C or G

&lt;400&gt; 170

```

acctgtgggc tgggctgtta tgctgtgcc ggctgtgaa agggagttca gaggtggagc      60
tcaaggagct ctgcaggcat tttgccaanc ctctccanag canagggagc aacctacact      120
ccccgctaga aagacaccag attggagtcc tgggaggggg agttgggggtg ggcatttgat      180
gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct      240
tcaaagctag gggctctggca ggtgga                                         266

```

&lt;210&gt; 171

&lt;211&gt; 1248

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1248)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 171

```

ggcagccaaa tcataaacgg cgaggactgc agcccgact cgcagccctg gcaggcggca      60
ctggctcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcacccgca gtgggtgctg      120
tcagccgcac actgtttcca gaagtgagtg cagagtcctt acaccatcgg gctgggcctg      180
cacagtcttg aggccgacca agagccaggg agccagatgg tggaggccag cctctccgta      240
cggcaccag agtacaacag acccttgctc gctaacgacc tcatgctcat caagttggac      300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc      360
gcggggaaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc      420
gtgctgcagt gcgtgaacgt gtggtgggtg tctgaggagg tctgcagtaa gctctatgac      480
ccgctgtacc accccagcat gttctgcgcc ggccggaggcc aagaccagaa ggactcctgc      540
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc      600
ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtc acaccaacct ctgcaaattc      660
actgagtgga tagagaaaac cgtccaggcc agttaactct ggggactggg aacctatgaa      720
attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agccccctct      780
ccctcaggcc caggagtcca ggccccccag ccctcctccc tcaaaccaag ggtacagatc      840
cccagccctt cctccctcag acccaggagt ccagaccccc cagccccctc tccctcagac      900
ccaggagtcc agccccctc cctcagacc caggagtcca gacccccag cccctcctcc      960
ctcagaccca ggggtccagg cccccaaccc ctctcctc agactcagag gtccaagccc      1020
ccaaccntc attccccaga cccagaggtc caggtcctcc cccctcntcc ctcagaccca      1080
gcgggtccaat gccacctaga ctntccctgt acacagtgcc cccttggtgc acgttgaccc      1140
aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt      1200
aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      1248

```

&lt;210&gt; 172

&lt;211&gt; 159

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(159)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 172

```

Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
 1           5           10           15
Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
          20          25          30
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
          35          40          45
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly

```

50		55		60
Arg Met Pro Thr Val	Leu Gln Cys Val	Asn Val Ser Val Val	Ser Glu	
65	70	75	80	
Glu Val Cys Ser Lys	Leu Tyr Asp Pro	Leu Tyr His Pro	Ser Met Phe	
	85	90	95	
Cys Ala Gly Gly Gln	Xaa Gln Xaa Asp	Ser Cys Asn Gly	Asp Ser	
	100	105	110	
Gly Gly Pro Leu Ile	Cys Asn Gly Tyr	Leu Gln Gly Leu	Val Ser Phe	
	115	120	125	
Gly Lys Ala Pro Cys	Gly Gln Val Gly	Val Pro Gly Val	Tyr Thr Asn	
	130	135	140	
Leu Cys Lys Phe Thr	Glu Trp Ile Glu	Lys Thr Val	Gln Ala Ser	
145	150	155		

<210> 173  
 <211> 1265  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1265)  
 <223> n = A,T,C or G

<400> 173					
ggcagccgc	actgcagcc	ctggcaggcg	gcactgggtca	tggaaaacga	attgttctgc 60
tggggcgctc	tggtgcatcc	gcagtgggtg	ctgtcagccg	cacactgttt	ccagaactcc 120
tacaccatcg	ggctgggcct	gcacagtctt	gaggccgacc	aagagccagg	gagccagatg 180
gtggaggcca	gcctctccgt	acggcaccca	gagtacaaca	gaccttgct	cgctaacgac 240
ctcatgctca	tcaagttgga	cgaatccgtg	tccgagtctg	acaccatccg	gagcatcagc 300
attgcttcgc	agtgccctac	cgcggggaac	tcttgccctg	tttctggctg	gggtctgctg 360
gcgaacgggtg	agctcacggg	tgtgtgtctg	ccctcttcaa	ggagggtcctc	tgcccagtcg 420
cgggggctga	cccagagctc	tgcgctccag	gcagaatgcc	taccgtgctg	cagtgcgtga 480
acgtgtcggt	ggtgtctgag	gaggctctga	gtaagctcta	tgaccgctg	taccacccca 540
gcatgttctg	cgccggcgga	gggcaagacc	agaaggactc	ctgcaacggg	gactctgggg 600
ggcccctgat	ctgcaacggg	tacttgacgg	gccttgtgtc	tttcggaaaa	gccccgtgtg 660
gccaagttgg	cgtgccaggt	gtctacacca	acctctgcaa	attcactgag	tggatagaga 720
aaaccgtcca	ggccagttaa	ctctggggac	tgggaaccca	tgaaattgac	ccccaaatac 780
atcctgcgga	aggaattcag	gaatatctgt	tcccagcccc	tcttccctca	ggcccaggag 840
tccaggcccc	cagcccctcc	tccctcaaac	caagggtaca	gatccccagc	ccctcctccc 900
tcagaccag	gagtcagac	ccccagccc	ctctcctc	agaccagga	gtccagcccc 960
tctcctca	gaccaggg	tccagacccc	ccagccctc	ctccctcaga	cccaggggtt 1020
gaggccccca	accctcctc	cttcagagtc	agagggtcaa	gcccccaacc	cctcgttccc 1080
cagaccaga	ggttnnaggtc	ccagccctc	ttcctcaga	cccagnggtc	caatgccacc 1140
tagattttcc	ctgnacacag	tgcccccttg	tggnangttg	acccaacctt	accagttggg 1200
ttttcatttt	tngtcccttt	cccctagatc	cagaaataaa	gtttaagaga	ngngcaaaaa 1260
aaaaa					1265

<210> 174  
 <211> 1459  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1459)  
 <223> n = A,T,C or G

&lt;400&gt; 174

ggtcagccgc	acactgtttc	cagaagttag	tgacagctc	ctacaccatc	gggctgggccc	60
tgacacagtct	tgaggccgac	caagagccag	ggagccagat	ggtaggaggcc	agcctctccg	120
tacggcacc	agagtacaac	agacccttgc	tcgctaacga	cctcatgtc	atcaagttgg	180
acgaatccgt	gtccgagtct	gacaccatcc	ggagcatcag	cattgcttcg	cagtgcacct	240
ccgcggggaa	ctcttgccctc	gtttctggct	ggggtctgct	ggcgaacggg	gagctcacgg	300
gtgtgtgtct	gccctcttca	aggaggtcct	ctgcccagtc	gcgggggctg	acccagagct	360
ctgctgcccc	ggcagaatgc	ctaccgtgct	gcagtgcgtg	aacgtgtcgg	tggtgtctga	420
ngaggtctgc	antaagctct	atgaccctgc	gtaccacccc	ancatgttct	gcgccggcgg	480
agggcaagac	cagaaggact	cctgcaacgt	gagagagggg	aaaggggagg	gcaggcgact	540
cagggaaggg	tggaagaagg	ggagacagag	acacacaggg	ccgcatggcg	agatgcagag	600
atggagagac	acacagggag	acagtgacaa	ctagagagag	aaactgagag	aaacagagaa	660
ataaacacag	gaataaagag	aagcaaagga	agagagaaac	agaaacagac	atggggaggc	720
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gacctccacc	caatagaaaa	tctctttata	acttttgact	ccccaaaaac	ctgactagaa	840
atagcctact	gttgacgggg	agccttacca	ataacataaa	tagtcgattt	atgcatacyl	900
tttatgcatt	catgatatac	ctttgttgga	attttttgat	atttctaagc	tacacagttc	960
gtctgtgaat	tttttttaaa	tgttgcaact	ctcctaaaaa	ttttctgatg	tgtttattga	1020
aaaaatccaa	gtataagtgg	acttgtgcat	tcaaacaggg	gttgttcaag	ggtcaactgt	1080
gtaccagag	ggaaacagtg	acacagattc	atagagggtga	aacacgaaga	gaaacaggaa	1140
aaatcaagac	tctacaagaa	ggctgggcag	ggtggctcat	gcctgtaate	ccagcacttt	1200
gggaggcgag	gcaggcagat	cacttgaggt	aaggagttca	agaccagcct	ggccaaaatg	1260
gtgaaatcct	gtctgtacta	aaaatacaaa	agttagctgg	atatgggtgg	aggcgccctgt	1320
aatcccagct	acttgggagg	ctgaggcagg	agaattgctt	gaatatggga	ggcagaggtt	1380
gaagtgaagt	gagatcacac	cactatactc	cagctggggc	aacagagtaa	gactctgtct	1440
caaaaaaaaa	aaaaaaaaaa					1459

&lt;210&gt; 175

&lt;211&gt; 1167

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (1167)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 175

gcgcagccct	ggcaggcggc	actgggtcatg	gaaaacgaat	tgttctgtct	gggcgtcctg	60
gtgcattccg	agtgggtgct	gtcagccgca	cactgtttcc	agaactccta	caccatcggg	120
ctgggectgc	acagtcttga	ggccgaccaa	gagccaggga	gccagatggt	ggaggccagc	180
ctctccgtac	ggcaccacaga	gtacaacaga	ctcttgtctg	ctaaccgacct	catgtctatc	240
aagttggacg	aatccgtgtc	cgagtctgac	accatccgga	gcacagcat	tgcttcgcag	300
tgccctaccg	cggggaactc	ttgcctcgtn	tctggctggg	gtctgctggc	gaacggcaga	360
atgcctaccg	tgctgcaactg	cgtgaacgtg	tcgggtgggt	ctgaggangt	ctgcagtaag	420
ctctatgacc	cgctgtacca	ccccagcatg	ttctgcccgg	gcggaggggca	agaccagaag	480
gactcctgca	acggtgactc	tgggggggccc	ctgatctgca	acgggtactt	gcagggcctt	540
gtgtctttcg	gaaaagcccc	gtgtggccaa	cttggcgtgc	caggtgtcta	caccaacctc	600
tgcaaatcca	ctgagtggat	agagaaaacc	gtccagncca	gttaactctg	gggactggga	660
acccatgaaa	ttgacccccca	aatacatcct	gcgggaangaa	ttcaggaata	tctgttccca	720
gcccctcctc	cctcaggccc	aggagtccag	gccccagcc	cctcctccct	caaaccaagg	780
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ccntcagacc	caggagtcca	gccccctcctc	cntcagacgc	aggagtccag	accccccagc	900
ccntctccg	tcagaccag	gggtgcaggc	ccccaaaccc	tcntccntca	gagtcagagg	960
tccaagcccc	caaccctcg	ttccccagac	ccagaggtn	aggtcccagc	ccctcctccc	1020
tcagaccag	cgggtccaatg	ccacctagan	tntccctgta	cacagtgc	ccttgygca	1080
ngttgacca	accttaccag	ttggtttttc	attttttgtc	cctttccct	agatccagaa	1140
ataaagtnta	agagaagcgc	aaaaaaa				1167

<210> 176  
 <211> 205  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1)...(205)  
 <223> Xaa = Any Amino Acid

<400> 176  
 Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp  
 1 5 10 15  
 Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu  
 20 25 30  
 Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val  
 35 40 45  
 Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu  
 50 55 60  
 Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser  
 65 70 75 80  
 Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly  
 85 90 95  
 Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met  
 100 105 110  
 Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val  
 115 120 125  
 Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala  
 130 135 140  
 Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly  
 145 150 155 160  
 Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys  
 165 170 175  
 Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys  
 180 185 190  
 Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser  
 195 200 205

<210> 177  
 <211> 1119  
 <212> DNA  
 <213> Homo sapien

<400> 177  
 gcgcactcgc agccctggca ggcggcactg gtcattggaaa acgaattggt ctgctcgggc 60  
 gtccctgggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctcctacacc 120  
 atcgggcttg gctgcacag tcttgaggcc gaccaagagc caggagacca gatggtggag 180  
 gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg 240  
 ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct 300  
 tcgcagtgcc ctaccgcggtg gaactcttgc ctctgttctg gctgggtct gctggcgaac 360  
 gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc 420  
 caaccctggc agggttgtac catttcggca acttcagtg caaggacgtc ctgctgcac 480  
 ctactcgggt gctcactact gtcactgca tcaccggaa cactgtgatc aactagccag 540  
 caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600  
 actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc 660  
 cagtatacct cactgaattg agatttctg cttcagtgtc agccattccc acataatttc 720  
 tgacctacag aggtgagggg tcatatagct cttcaaggat gctggtactc cctcacaaa 780

```

ttcattttctc ctgtttagt gaaaggtgcg ccctctggag cctcccaggg tgggtgtgca      840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg      900
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca      960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg     1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc     1080
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaaa     1119

```

<210> 178  
 <211> 164  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1) ... (164)  
 <223> Xaa = Any Amino Acid

```

<400> 178
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1          5          10          15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
          20          25          30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
          35          40          45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
          50          55          60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
65          70          75          80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
          85          90          95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
          100         105         110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
          115         120         125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
          130         135         140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
145         150         155         160
Pro Gly Thr Leu

```

<210> 179  
 <211> 250  
 <212> DNA  
 <213> Homo sapien

```

<400> 179
ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct      60
ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct      120
gccaggcact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgctga      180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa      240
aaaaaaaaaa                                     250

```

<210> 180  
 <211> 202  
 <212> DNA  
 <213> Homo sapien



<400> 180  
 actagtccag tgtggtggaa ttccattgtg ttggggcccaa cacaatggct acctttaaca 60  
 tcacccagac cccgcccctg cccgtgcccc acgctgctgc taacgacagt atgatgctta 120  
 ctctgtact cggaactat ttttatgtaa ttaatgtatg ctttcttggt tataaatgcc 180  
 tgatttaaaa aaaaaaaaaa aa 202

<210> 181  
 <211> 558  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (558)  
 <223> n = A,T,C or G

<400> 181  
 tccytttgkt naggtttkkg agacamccck agacctwaan ctgtgtcaca gacttcyngg 60  
 aatgtttagg cagtgtagt aatttcytcg taatgattct gttattactt tccnattct 120  
 ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa 180  
 ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca 240  
 aaattatgca agttagtaat tactcaggtt taactaaatt actttaatat gctgttgaaac 300  
 ctactctgtt ccttggttag aaaaaattat aaacaggact ttgttagttt gggaagccaa 360  
 attgataata ttctatgttc taaaagttag gctatacata aattattaag aaatatggaw 420  
 ttttattccc aggaatatgg kgttcathtt atgaatatta cscrggatag awgtwtgagt 480  
 aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc 540  
 caaaaaaaaa aaaaaaaaaa 558

<210> 182  
 <211> 479  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (479)  
 <223> n = A,T,C or G

<400> 182  
 acagggwttk grgatgcta agscccrga rwtggttga tccaaccctg gcttwttttc 60  
 agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcmgt gcacccctgg 120  
 cstcacacag astcccgagt agctgggact acaggcacac agtcactgaa gcaggccctg 180  
 ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca 240  
 ctaaggttaa actttccac ccagaaaagg caacttagat aaaatcttag agtactttca 300  
 tactmttcta agtctcttcc cagcctcact kkgagtcctm cytgggggtt gataggaant 360  
 ntctcttggc tttctcaata aartctctat ycatctcatg tttaatttgg tacgcatara 420  
 awtgstgara aaattaaaaat gttctggtty mactttaaaa aaaaaaaaaa aaaaaaaaaa 479

<210> 183  
 <211> 384  
 <212> DNA  
 <213> Homo sapien

<400> 183  
 aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc 60  
 agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtgggtg cttcagtgtc 120  
 ggtgccagcc tgaccgccac tctcacattt gggtctcttc ctggccttgg tggagctggt 180  
 gccagcacca gtggcagctc tgggtgcctgt ggtttctcct acaagtgaga ttttagatat 240

```

tgtaatacct gccagtcctt ctcttcaagc cagggtgcat cctcagaaac ctactcaaca    300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctatct    360
gccatttcaa aaaaaaaaaa aaaa                                           384

```

<210> 184

<211> 496

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(496)

<223> n = A,T,C or G

<400> 184

```

accgaattgg gaccgctggc ttataagcga tcatgttynt ccrgtatcac ctcaacgagc    60
aggagatcgc agtctatacg ctgaagaaat ttgacccgat gggacaacag acctgctcag    120
cccatcctgc tccgttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga    180
aacgcttcaa ggtgctcatg acccagcaac cgcgcctgt cctctgaggg tcccttaaac    240
tgatgtcttt tctgccacct gttacccctc ggagactccg taaccaaact ctccggactg    300
tgagccctga tgcctttttg ccagccatac tctttggcat ccagtctctc gtggcgattg    360
attatgcttg tctgaggcaa tcatggtggc atcacccata aagggaacac atttgacttt    420
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaaaaactst    480
taaaaaaaaa aaaaaa

```

<210> 185

<211> 384

<212> DNA

<213> Homo sapien

<400> 185

```

gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agtgacttcc    60
caagtatcyt ggcsgcgctc ttctaccgtc cctacctgca gatcttcggg cagattcccc    120
aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggettct    180
gggcacacc tccgtgggccc caggcgggca cctgcgtctc ccagtatgcc aactggcttg    240
tgggtgctgt cctcgtcatc ttctgctcgc tggccaacat cctgctggtc aacttgctca    300
ttgccatgtt cagttacaca ttccggcaaag tacagggcaa cagcgatctc tactgggaag    360
gcgcagcgtt accgcctcat ccgg

```

<210> 186

<211> 577

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(577)

<223> n = A,T,C or G

<400> 186

```

gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggctctctgc ttcataccgc    60
tnccatcgct atactgtagg ttggccacca cytcctggca tcttggggcg gcntaatatt    120
ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggtggttc tgtcttcgcg    180
tcggtgtgaa aggatctccc agaaggagtg ctcgatcttc cccacacttt tgatgacttt    240
attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgaggtcac    300
cagccctatc atgccgttga mcgtgccgaa gartaccgag ccttgtgttg gggkkgaagt    360
ctaccccaga ttctgcatta ccagagagcc gtggcaaaaag acattgacaa actcgcccag    420
gtggaaaaag amcamctcct ggargtgctn gccgctcttc gtcmgttggt ggcagcgctw    480

```

tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcacatcc 540  
aagatntcgc acagcactna tccagttggg attaaat 577

<210> 187

<211> 534

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(534)

<223> n = A,T,C or G

<400> 187

aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaaticatw	60
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact	120
ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagctctggg aakaagggtg	180
tgccctattc acacctgtta aaaggcgct aagcattttt gattcaacat cttttttttt	240
gacacaagtc cgaacaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc	300
ttcatgggac agagccatyt gatttaaaaa gcaaattgca taatattgag ctttygggagc	360
tgatatttga gcggaagagt agcctttcta cttcaccaga cacaactccc tttcatattg	420
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa ttctgttctg	480
aggatctccc agttatttta ccacttgcac aagaaggcgt tttcttctc aggc	534

<210> 188

<211> 761

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(761)

<223> n = A,T,C or G

<400> 188

agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaatth tgtgtgcgtg	60
tgtgtgtgcg cgcataattat atagacaggc acatcttttt tacttttgta aaagcttatg	120
cctcttttgt atctatatct gtgaaagttt taatgatctg ccataatgac ttggggacct	180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagtngt	240
tttattcgac atgaaggaaa tttccagatn acaactna caaactctcc ctkgackarg	300
ggggacaaag aaaagcaaaa ctgamcataa raaacaatwa cctgggtgaga arttgcataa	360
acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgtttwtktt wttctccctt	420
gcaaaaaaca tgtacngact tcccgttgag taatgccaaag ttgttttttt tatnataaaa	480
cttgcccttc attacatggt tnaaagtggg gtgggtggcc aaaatattga aatgatggaa	540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac	600
atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaataca ctttgaacta	660
tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac	720
gaaaaataata acattgaaga aaaananaaa aaanaaaaaa a	761

<210> 189

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(482)

<223> n = A,T,C or G

&lt;400&gt; 189

tttttttttt	tttgccgatn	ctactatttt	attgcaggan	gtgggggtgt	atgcaccgca	60
caccggggct	atnagaagca	agaaggaagg	agggagggca	cagccccttg	ctgagcaaca	120
aagccgcctg	ctgccttctc	tgtctgtctc	ctgggtgcagg	cacatgggga	gaccttcccc	180
aaggcagggg	ccaccagtcc	aggggtggga	atacaggggg	tgggagtgt	gcataagaag	240
tgataggcac	aggccacccg	gtacagacct	ctcggtcct	gacaggtnga	tttcgaccag	300
gtcattgtgc	cctgcccagg	cacagcgtn	atctggaaaa	gacagaatgc	tttccttttc	360
aaatttggt	ngtcatngaa	ngggcanttt	tccaantng	gctnggtctt	ggtacncttg	420
gttcggccca	gtccnctgc	caaaaantat	tcaccnct	ccnaattgct	tgcnggnccc	480
cc						482

&lt;210&gt; 190

&lt;211&gt; 471

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(471)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 190

tttttttttt	ttttaaaaca	gtttttcaca	acaaaattta	ttagaagaat	agtggttttg	60
aaaactctcg	catccagtga	gaactacat	acaccacatt	acagctngga	atgtntctcca	120
aatgtctggt	caaatgatac	aattggaacca	ttcaatctta	cacatgcacg	aaagaacaag	180
cgcttttgac	atacaatgca	caaaaaaaaa	aggggggggg	gaccacatgg	attaaaattt	240
taagtactca	tcacatacat	taagacacag	ttctagtcca	gtcnaaaatc	agaactgcnt	300
tgaaaaattt	catgtatgca	atccaaccaa	agaacttnat	tggtgatcat	gantnctcta	360
ctacatcnac	cttgatcatt	gccaggaacn	aaaagttnaa	ancacnngt	acaaaaanaa	420
tctgtaattn	anttcaacct	ccgtacngaa	aatnttnnt	tatacactcc	c	471

&lt;210&gt; 191

&lt;211&gt; 402

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(402)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 191

gagggattga	aggtctgttc	tastgtcggm	ctgttcagcc	accaactcta	acaagttgct	60
gtcttccact	cactgtctgt	aagcttttta	accagacwg	tatcttcata	aatagaacaa	120
attcttcacc	agtcacatct	tctaggacct	ttttggattc	agttagtata	agctcttcca	180
cttcctttgt	taagacttca	tctggtaaag	tcttaagttt	tgtagaaagg	aattyaattg	240
ctegtctct	aacaatgtcc	tctccttgaa	gtatttggt	gaacaaccca	cctaaagtcc	300
ctttgtgcat	ccatttttaa	tatacttaat	agggcattgk	tnactaggt	taaattctgc	360
aagagtcatc	tgtctgcaaa	agttgcgtta	gtatatctgc	ca		402

&lt;210&gt; 192

&lt;211&gt; 601

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (601)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 192

```
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact      60
gggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac      120
atgcytyttt gaytaccgtg tgccaagtgc tgggtattct yaacacacyt ccatcccggt      180
cttttgtgga aaaactggca cttktctgga actagcarga catcacttac aaattcaccc      240
acgagacact tgaaagggtg aacaaagcga ytcttgcat gctttttgtc cctccggcac      300
cagttgtcaa tactaaccgg ctggtttgcc tccatcacat ttgtgatctg tagctctgga      360
tacatctcct gacagtactg aagaacttct tcttttgttt caaaagcarg tcttggtgcc      420
tgttggatca ggttcccatt tcccagtcyg aatgttcaca tggcatattt wacttcccac      480
aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag      540
cctcgatgta gccggccagc gccaaaggcag gcgccgtgag cccaccagc agcagaagca      600
g
```

601

&lt;210&gt; 193

&lt;211&gt; 608

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (608)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 193

```
atacagcca natcccacca cgaagatgcg cttgttgact gagaacctga tgcggtcact      60
gggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt      120
cccaacgcag gcagmagcgg gscgggtcaa tgaactccay tctgtgcttg gggtkgacgg      180
tkaagtgcag gaagaggctg accacctcgc ggtccaccag gatgcccgac tgtgcgggac      240
ctgcagcgaa actcctcgat ggtcatgagc gggaagcgaa tgaggccag ggccttgccc      300
agaaccttcc gctgtttctc tggcgtcacc tgcagctgct gccgctgaca ctggcctcg      360
gaccagcgga caaacggcrt tgaacagccg cacctcacgg atgccagtg tgcgcgctc      420
caggammgsc accagcgtgt ccagggtcaat gtccggtgaag cctcccgcg gtrattggcg      480
ctgcagtggt tttgtcgatg ttctccaggc acaggctggc cagctgcggt tcatcgaaga      540
gtcgcgctg cgtgagcagc atgaaggcgt tgcgggctcg cagttcttct tcagggaactc      600
cacgcaat
```

608

&lt;210&gt; 194

&lt;211&gt; 392

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (392)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 194

```
gaacggctgg acctgcctc gcattgtgct tgctggcagg gaataccttg gcaagcagyt      60
ccagtcggag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc      120
tccgcctcaa tgcagaacca gtatggggag cactgtgttt agagttaaga gtgaacactg      180
tttgatttta cttgggaatt tcctctgtta tatagctttt ccaatgcta atttccaaac      240
aacaacaaca aaataacatg tttgcctgtt aagttgtata aaagtaggtg attctgtatt      300
taaagaaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktncstggt      360
aaataaatat agttattaaa ggttgtcant cc
```

392

<210> 195  
 <211> 502  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(502)  
 <223> n = A,T,C or G

<400> 195  
 ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg 60  
 ccgagctgag gcagatgttc ccacagtgc cccagagacc stgggstata gtytctgacc 120  
 cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc 180  
 aagggaaagg cccattccgg ggstgttccc cgaggaggaa gggaaagggc tctgtgtgcc 240  
 ccccasgagg aagaggccct gagtccctgg atcagacacc ccttcacgtg tatccccaca 300  
 caaatgcaag ctcaccaagg tccccctcga gtcccccttc stacaccctg amcggccact 360  
 gscscacacc caccagagc acgccacccg ccattggggar tgtgtctcaag gartcgcnng 420  
 gcarcgtgga catctngtcc cagaaggggg cagaatctcc aatagangga ctgarcmstt 480  
 gctnanaaaa aaaaaaaaaa aa 502

<210> 196  
 <211> 665  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(665)  
 <223> n = A,T,C or G

<400> 196  
 gggtacttgg ttctattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60  
 cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact gctgaatttt 120  
 wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga 180  
 actwatattat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkac 240  
 aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt 300  
 attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgaact 360  
 tcacttggtt attttattgt aaatgartta caaaattctt aatttaagar aatggatgt 420  
 watatttatt tcattaattt ctttcctkgt ttacgtwaat ttgaaaaga wtgcatgatt 480  
 tcttgacaga aatcgatctt gatgctgtgg aagtagtttg acccacatcc ctatgagttt 540  
 ttcttagaat gtataaagggt tgtagcccat cnaacttcaa agaaaaaat gaccacatac 600  
 tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan 660  
 aagtg 665

<210> 197  
 <211> 492  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(492)  
 <223> n = A,T,C or G

<400> 197  
 tttntttttt ttttttttgc aggaaggatt ccatttattg tggatgcatt ttcacaatat 60  
 atgtttattg gagcgatcca ttatcagtga aaagtatcaa gtgtttataa natttttagg 120

```

aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtana gatnacagag      180
aattatagtc naaccagtaa acnaggaatt tactttttcaa aagattaaat ccaaactgaa      240
caaaattcta ccctgaaact tactccatcc aaatattgga ataanagtca gcagtgatac      300
attctcttct gaactttaga ttttctagaa aaatatgtaa tagtgatcag gaagagctct      360
tgttcaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc      420
catttcactc ccatacggg agtcaatgct acctgggaca cttgtatttt gttcatnctg      480
ancntggctt aa
                                         492

```

&lt;210&gt; 198

&lt;211&gt; 478

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (478)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 198

```

ttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa      60
tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac      120
tgagtatatt ttgaaaagga caagtttaaa gtanacncat attgccganc atancacatt      180
tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaanaaat      240
natatatgtc aatcngattt aagatacaaa acagatccta tggtagatan catcntgtag      300
gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta      360
agcattctag tacctctact ccatggttaa gaatcgtaca cttatgttta catatgtntca      420
gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa      478

```

&lt;210&gt; 199

&lt;211&gt; 482

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (482)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 199

```

agtgacttgt cctccaacaa aacccttga tcaagtttgt ggcactgaca atcagaccta      60
tgctagttcc tgcctcttat tcgctactaa atgcagactg gagggggacca aaaaggggca      120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga      180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta      240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga      300
aaatttacct ggangaaaag aggctttngg ctggggacca tcccattgaa ccttctctta      360
anggacttta agaanaaaact accacatgtn tgtngtatcc tgggtgcngg ccgtttantg      420
aacntngaen ncacccttnt ggaatanant cttgacngcn tctgaactt gctcctctgc      480
ga
                                         482

```

&lt;210&gt; 200

&lt;211&gt; 270

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (270)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 200

```

cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgccca gcagttgggtc      60
cgactgcgac gacggcggcg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc      120
aaggetgagc tgacgccgca gaggtcgtgt cacgtcccac gacettgacg ccgtcgggga      180
cagccggaac agagcccgtt gaangcggga ggcctcgggg agccctcggg gaaggcgggc      240
ccgagagata cgcaggtgca ggtggccgcc

```

270

&lt;210&gt; 201

&lt;211&gt; 419

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(419)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 201

```

tttttttttt ttttggaaac tactgcgagc acagcaggtc agcaacaagt ttatatttgc      60
gctagcaagg taacagggtta gggcatgggt acatgttcag gtcaacttcc tttgtcgtgg      120
ttgattggtt tgtctttatg ggggcggggt ggggtagggt aaancgaagc anaantaaca      180
tggagtgggt gcaccctccc tgtagaacct gggtacnaaa gcttggggca gttcacctgg      240
tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatata ttttagagag      300
tccactgtnt ctggagggag attaggggtt cttgccanaa tccaancaa atccacntga      360
aaaagttgga tgatncangt acngaatacc ganggcatan ttctcatant cggtggcca      419

```

&lt;210&gt; 202

&lt;211&gt; 509

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(509)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 202

```

tttntttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt      60
tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng      120
gtnattttnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaatnnaa      180
tacnncnaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaattaaaaa      240
aatatatacg gctgggtgtt tcaaagtaca attatcttaa cactgcaaac atnttttnnaa      300
ggaactaaaa taataaaaaa cactnccgca aagggttaaag ggaacaacaa attcntttta      360
caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng      420
ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca      480
caatggnaat nccnccnncn tggactagt

```

509

&lt;210&gt; 203

&lt;211&gt; 583

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(583)

&lt;223&gt; n = A,T,C or G



&lt;400&gt; 203

tttttttttt	ttttttttga	ccccctctt	ataaaaaaca	agttaccatt	ttattttact	60
tacacatatt	tattttataa	ttggtattag	atattcaaaa	ggcagctttt	aaaatcaaac	120
taaatggaaa	ctgccttaga	tacataattc	ttaggaatta	gcttaaaaac	tgcctaaagt	180
gaaaatcttc	tctagctctt	ttgactgtaa	atttttgact	cttgtaaaac	atccaaattc	240
atttttcttg	tctttaaaat	tatctaattc	ttccattttt	tcctatttcc	aagtcaattt	300
gcttctctag	cctcatttcc	tagctcttat	ctactattag	taagtggctt	ttttcctaaa	360
agggaaaaca	ggaagagana	atggcacaca	aaacaaacat	tttatattca	tatttctacc	420
tacgttaata	aaatagcatt	ttgtgaagcc	agctcaaaag	aaggcttaga	tccttttatg	480
tccatttttag	tcactaaacg	atatcnaaag	tgccagaatg	caaaagggtt	gtgaacattt	540
attcaaaagc	taatataaga	tatttcacat	actcatcttt	ctg		583

&lt;210&gt; 204

&lt;211&gt; 589

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(589)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 204

ttttttttnt	tttttttttt	ttttttntct	ttcttttttt	ttganaatga	ggatcgagtt	60
tttactcttc	tagatagggc	atgaagaaaa	ctcatctttc	cagcttttaa	ataacaatca	120
aatctcttat	gctatatcat	atttttaagt	aaactaatga	gtcactggct	tatcttctcc	180
tgaaggaaat	ctgttcattc	ttctcattca	tatagttata	tcaagtacta	ccttgcatat	240
tgagagggtt	ttcttctcta	tttacacata	tatttccatg	tgaatttgta	tcaaaccctt	300
attttcatgc	aaactagaaa	ataatgtntt	cttttgcata	agagaagaga	acaatatnag	360
cattacaaaa	ctgctcaaat	tgtttgttaa	gnntatccat	tataattagt	tnggcaggag	420
ctaatacaaa	tcacattttac	ngacnagcaa	taataaaaact	gaagtaccag	ttaaatatcc	480
aaaataatta	aaggaacatt	tttagcctgg	gtataattag	ctaattcact	ttacaagcat	540
ttattnagaa	tgaattcaca	tgttattatt	centagccca	acacaatgg		589

&lt;210&gt; 205

&lt;211&gt; 545

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(545)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 205

ttttnttttt	ttttttcagt	aataatcaga	acaatatatta	tttttatatt	taaaattcat	60
agaaaagtgc	cttacattta	ataaaagttt	gtttctcaaa	gtgatcagag	gaattagata	120
tngtcttgaa	caccaatatt	aatttgagga	aaatacacca	aaatacatta	agtaaattat	180
ttaagatcat	agagcttgta	agtgaaaaaga	taaaatttga	cctcagaaac	tctgagcatt	240
aaaaatccac	tattagcaaa	taaattacta	tggacttctt	gctttaattt	tgtgatgaat	300
atgggggtgc	actgggtaaac	caacacattc	tgaaggatac	attacttagt	gatagattct	360
tatgtacttt	gctanatnac	gtggatatga	gttgacaagt	ttctctttct	tcaatctttt	420
aaggggcnga	ngaaatgagg	aagaaaagaa	aaggattacg	catactgttc	tttctatngg	480
aaggattaga	tatgtttcct	ttgccaatat	taaaaaata	ataatgttta	ctactagtga	540
aacc						545

&lt;210&gt; 206

&lt;211&gt; 487

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(487)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 206

tttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttggtcattt	60
cattttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna	120
caattttataa atgtaagggtg ccattattga gtanatatat tcctccaaga gtggatgtgt	180
ccctttctccc accaactaat gaancagcaa cattagttta attttattag tagatnatac	240
actgttgcaa acgctaattc ttttctccat ccccatgtng atattgtgta tatgtgtgag	300
ttggttnagaa tgcatacanca atctnacaat caacagcaag atgaagctag gcntgggctt	360
tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cggtggcaag	420
aactcttcga accgcttcct caaaggcngc tgccacattt gtggcntctn ttgcacttgt	480
ttcaaaa	487

&lt;210&gt; 207

&lt;211&gt; 332

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(332)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 207

tgaattggct aaaagactgc atttttanaa ctagcaactc ttattttcttt cctttaaaaa	60
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggctcactact	120
gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana	180
atctttgcat gcagaggagg taaaagggtat tggattttca cagaggaana acacagcgca	240
gaaatgaagg ggccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg	300
aaaagaaggc agcctaggcc ctggggagcc ca	332

&lt;210&gt; 208

&lt;211&gt; 524

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(524)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 208

agggcggtgt gcggagggcg ttactgtttt gtctcagtaa caataaatac aaaaagactg	60
gttggtgtcc ggccccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat	120
tttaaaggac atggagcttg tcacaatgtc acaatgtcac agtggtgaagg gcacactcac	180
tcccgcgtga ttcacattta gcaaccaaca atagctcatg agtccatact tgtaaatact	240
tttggcagaa tacttnttga aacttgcaga tgataactaa gatccaagat atttcccaaa	300
gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaagtc	360
atgagcccag aactgacat caaactaagc ccacttagac tcctcaccac cagtctgtcc	420
tgatcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa	480
aaaccattac ctgatccact tccggtaatg caccaccttg gtga	524

<210> 209  
 <211> 159  
 <212> DNA  
 <213> Homo sapien

<400> 209  
 ggggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgtccttg 60  
 tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca 120  
 caaaggactc tcgacccaaa ctgccccaga ccctctcca 159

<210> 210  
 <211> 256  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (256)  
 <223> n = A,T,C or G

<400> 210  
 actccctggc agacaaaggc agaggagaga gctctgtag ttctgtgttg ttgaactgcc 60  
 actgaatttc tttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta 120  
 tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat 180  
 ttgcagggtg naaatgggan ggctgggttg ttanatgaac agggacatag gaggtaggca 240  
 ccaggatgct aatca 256

<210> 211  
 <211> 264  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (264)  
 <223> n = A,T,C or G

<400> 211  
 acattgtttt tttagataa agcattgaga gagctctcct taacgtgaca caatggaagg 60  
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120  
 atattcaagc acatatgtta tatattatc agttccatgt ttatagccta gttaaggaga 180  
 ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga 240  
 aaaaaggag caaatgagaa gcct 264

<210> 212  
 <211> 328  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (328)  
 <223> n = A,T,C or G

<400> 212  
 acccaaaaat ccaatgctga atatttggtc tcattattcc canattcttt gattgtcaaa 60  
 ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag 120  
 gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag 180

ttnaatttca ttccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta 240  
 cccctacnac tctttactct ctgganaggg ccagtgggtg tagctataag cttggccaca 300  
 ttttttttct cttttattct ttgtcaga 328

<210> 213

<211> 250

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(250)

<223> n = A,T,C or G

<400> 213

acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt 60  
 taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct 120  
 cattatgcca aagganatat acatttcaat tctccaaact tcttctcat tccaagagtt 180  
 ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatata tctctnacct 240  
 tctcatcggt 250

<210> 214

<211> 444

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(444)

<223> n = A,T,C or G

<400> 214

accagaatc caatgctgaa tatttggett cattattccc agattctttg attgtcaaag 60  
 gatttaattg tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg 120  
 tttatatatg cagcaacaat attcaagcgc gacaacaggc tattgaactt gcccgccagt 180  
 tgaatttcat tccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac 240  
 ccctacgact ctttactctc tggagagggc cagtgggtgg agctataagc ttggccacat 300  
 ttttttttcc tttattcctt tgtcagagat gcgattcacc catatgctan aaaccaacag 360  
 agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt 420  
 actttgctct ccctaataata cctc 444

<210> 215

<211> 366

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(366)

<223> n = A,T,C or G

<400> 215

acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt 60  
 taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct 120  
 cattatgcca aagganatat acatttcaat tctccaaact tcttctcat tccaagagtt 180  
 ttcaatattt gcatgaacct gctgataagc catgttgaga aacaaatata tctctgacct 240  
 tctcatcggt aagcagaggc tgtaggcaac atggaccata gcgaanaaaa aacttagtaa 300  
 tccaagctgt tttctacact gtaaccaggt ttccaaccaa ggtggaaatc tctataactt 360

ggtgcc

366

&lt;210&gt; 216

&lt;211&gt; 260

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(260)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 216

ctgtataaac	agaactccac	tgcanagagg	agggccgggc	caggagaatc	tccgcttgtc	60
caagacaggg	gcctaaggag	ggtctccaca	ctgctnntaa	gggctnttnc	atTTTTTtat	120
taataaaaag	tnnaaaaggc	ctcttctcaa	ctTTTTTccc	ttnggctgga	aaatttaaaa	180
atcaaaaatt	tctnaagtt	ntcaagctat	catatatact	ntatcctgaa	aaagcaacat	240
aattcttctt	tccctccttt					260

&lt;210&gt; 217

&lt;211&gt; 262

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(262)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 217

acctacgtgg	gtaagtttan	aaatgttata	atttcaggaa	naggaacgca	tataattgta	60
tcttgccat	aattttctat	tttaataagg	aaatagcaaa	ttgggggtggg	gggaatgtag	120
ggcattctac	agtttgagca	aaatgcaatt	aaatgtggaa	ggacagcact	gaaaaatttt	180
atgaataatc	tgtatgatta	tatgtctcta	gagtagattt	ataattagcc	acttaccta	240
atatccttca	tgcttgtaaa	gt				262

&lt;210&gt; 218

&lt;211&gt; 205

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(205)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 218

accaaggtgg	tgcatcaccg	gaantggatc	aangacacca	tctgtggccaa	cccctgagca	60
cccctatcaa	ctcccttttg	tagtaaactt	ggaaccttgg	aaatgaccag	gccaagactc	120
aggcctcccc	agttctactg	acctttgtcc	ttangnttna	ngtccagggt	tgctaggaaa	180
anaaatcagc	agacacaggt	gtaaa				205

&lt;210&gt; 219

&lt;211&gt; 114

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 219

tactgttttg tctcagtaac aataaatatac aaaagactgg ttgtgttccg gccccatcca 60  
accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga 114

<210> 220  
<211> 93  
<212> DNA  
<213> Homo sapien

<400> 220  
actagccagc acaaaaggca gggtagcctg aattgctttc tgctctttac atttctttta 60  
aaataagcat ttagtgctca gtccctactg agt 93

<210> 221  
<211> 167  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(167)  
<223> n = A,T,C or G

<400> 221  
actangtgca ggtg'gcaca aatatttgct gatattccct tcatcttgga ttccatgagg 60  
tcttttgccc agcctgtggc tctactgtag taagtttctg ctgatgagga gccagnatgc 120  
ccccactac cttccctgac gctcccccana aatcacccaa cctctgt 167

<210> 222  
<211> 351  
<212> DNA  
<213> Homo sapien

<400> 222  
agggcgtggt gcggagggcg gtactgacct cattagtagg aggatgcatt ctggcacccc 60  
gttcttcacc tgtcccccac tccttaaaag gccatactgc ataaagtcaa caacagataa 120  
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180  
ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt 240  
taggtgagca tgattagaga gcttgtaggt tgcttttaca tatactctggc atatttgagt 300  
ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t 351

<210> 223  
<211> 383  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(383)  
<223> n = A,T,C or G

<400> 223  
aaaacaaaca acaaaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat 60  
tggtaattat ggtcaattta atwrtrttkt ggggcatttc cttacattgt cttgacaaga 120  
ttaaagtgc tgtgccaaaa ttttgatttt tatttgagga cttcttatca aaagtaatgc 180  
tgccaaagga agtctaagga attagtagtg ttcccmtcac ttggttgagg tgtgctattc 240  
taaaagattt tgatttctctg gaatgacaat tatattttta clttgggtggg ggaaanagtt 300  
ataggaccac agtcttcact tctgatactt gtaaatattt cttttattgc acttgttttg 360  
accattaagc tatatgttta aaa 383

<210> 224  
 <211> 320  
 <212> DNA  
 <213> Homo sapien

<400> 224  
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 ggatacatgg ttaaaggata raagggaat attttatcat atgttctaaa agagaaggaa 180  
 gagaaaatac tactttctcr aaatggaagc ccttaaagggt gctttgatac tgaaggacac 240  
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 tttaractcm gcattgtgac 320

<210> 225  
 <211> 1214  
 <212> DNA  
 <213> Homo sapien

<400> 225  
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 aactcctaca ccacggggt gggcctgcac agtcttgagg ccgaccaaga gccagggagc 180  
 cagatggtgg aggccagcct ctccgtacgg caccagagt acaacagacc cttgctcgtc 240  
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 gaggaggtct gcagtaagct ctatgaccg ctgtaccacc ccagcatgtt ctgcgcgggc 480  
 ggagggcaag accagaagga ctctgcaac ggtgactctg gggggcccct gatctgcaac 540  
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 cagtgcctcc ttgtggcacg ttgacccaac cttaccagtt ggtttttcat tttttgtccc 1140  
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 aaaaaaaaaa aaaa 1214

<210> 226  
 <211> 119  
 <212> DNA  
 <213> Homo sapien

<400> 226  
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 agaacctggc ccagtcataa tcattcatcc tgacagtggc aataatcacg ataaccagt 119

<210> 227  
 <211> 818  
 <212> DNA  
 <213> Homo sapien

<400> 227  
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aattttcctc	ctctggagga	aagggtggtga	ttgacaggca	gggagacagt	gacaaggcta	240
gagaaagcca	cgctcggcct	tctctgaacc	aggatggaac	ggcagacccc	tgaaaacgaa	300
gcttgtcccc	ttccaatcag	ccacttctga	gaaccccat	ctaacttcct	actggaaaag	360
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gacaggtctt	gcctcaagc	cggctgaggg	cagcaaccac	tctcctcccc	tttctcacgc	660
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caagaggata	tgaggactgt	ctcagcctgg	ctttgggctg	acaccatgca	cacacacaag	780
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&lt;210&gt; 228

&lt;211&gt; 744

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 228

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tcgtggccga	cctggcctct	cctggcctgt	ttcttaagat	gcggagtcac	atttcaatgg	180
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accagattct	aggccagttt	gttccactga	agcttttccc	acagcagtc	acctctgcag	360
gctggcagct	gaatggcttg	ccgggtggctc	tgtggcaaga	tcacactgag	atcgatgggt	420
gagaaggcta	ggatgcttgt	ctagtgttct	tagctgtcac	gttggctcct	tccaggttgg	480
ccagacgggtg	ttggccactc	ccttctaaaa	cacaggcgcc	ctcctggtga	cagtgacccg	540
ccgtgggtatg	ccttggccca	ttccagcagt	cccagttatg	catttcaagt	ttggggtttg	600
ttcttttcgt	taatgttctt	ctgtgttgtc	agctgtcttc	atttctctgg	ctaagcagca	660
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cttactctg	aagtagctgg	tggt				744

&lt;210&gt; 229

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 229

cgagctctggg	ttttgtctat	aaagtgtgat	ccctcctttt	ctcatccaaa	tcagtgaac	60
cattacacat	cgaaataaaa	gaaaggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
tgcagggttg	ttgtttttta	attattattg	ttagaaacgt	caccacagct	ccctgttaat	180
ttgtatgtga	cagccaactc	tgagaaggtc	ctatttttcc	acctgcagag	gatccagctt	240
cactaggctc	ctccttgccc	tcacactgga	gtctccgcca	gtgtgggtgc	ccactgacat	300

&lt;210&gt; 230

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 230

cagcagaaca	aatacaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
gagcgacagt	tcaaggagga	gaagcttgca	gagcagctca	agcaagctga	ggagctcagg	120
caatataaag	tcctggttca	cactcaggaa	cgagagctga	cccagttaag	ggagaagtgg	180
cggggaaggga	gagatgcctc	cctctcattg	aatgagcatc	tccaggccct	cctcactccg	240
gatgaaccgg	acaagtccca	ggggcaggac	ctccaagaaa	cagacctcgg	ccgcgaccac	300
g						301



<210> 231  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 231  
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 caggaactcc aagtccacat ccttggcaac tggggacttg cgcaggttag ccttgaggat 120  
 ggcaacacgg gacttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg 180  
 tctgaggatg gcaggatcaa tgatgtcagg ccggttggtg ccgccaatga tgaacacatt 240  
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 c 301

<210> 232  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 232  
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 agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtctgttcca 180  
 cgtgctgtac caagtgtctg tgccagcctg ttacctgttc tcaactgaaa tctggctaata 240  
 gctcttgtgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300  
 g 301

<210> 233  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 233  
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 cctagaagtt acagagcatc tagctggtgc gctggcacc cttggcctcac acagactccc 180  
 gagtagctgg gactacaggc acacagtcac tgaagcaggc cctgttagca attctatgcg 240  
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 c 301

<210> 234  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 234  
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 tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct 180  
 cgctcatga cagcaagttc aatgtttttg ccacctgact gaaccacttc caggagtgcc 240  
 ttgatcacca gcttaatggg cagatcatct gtttcaatgg ctctgctcagt atagttcttc 300  
 t 301

<210> 235  
 <211> 283  
 <212> DNA  
 <213> Homo sapien

&lt;400&gt; 235

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aattccctca tcttttaggg aatcatttac caggtttgga gaggattcag acagctcagg	120
tgctttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaata	180
atgttatctt tgaactgatg ctcataggag agaataaag aactctgagt gatatcaaca	240
ttagggattc aaagaaatat tagatttaag ctacactgg tca	283

&lt;210&gt; 236

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 236

aggtcctcca ccaactgcct gaagcacggt taaaattggg aagaagtata gtgcagcata	60
aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg	120
tcggagcagc atcattaata ccaagcagaa tgcgtaatag ataaatacaa tggatatatag	180
tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta	240
aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc	300
a	301

&lt;210&gt; 237

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 237

cagtggtagt ggtggaggac gtggcggttg tcgtgggtgcc ttttttggtg cccgtcacaa	60
actcaatttt tgttcgctcc tttttggcct tttccaattt gtccatctca attttctggg	120
ccttggttaa tgcctcatag taggagtcct cagaccagcc atggggatca aacatacct	180
ttgggtagtt ggtgccaagc tcgtcaatgg cacagaatgg atcagcttct cgtaaatcta	240
gggttccgaa attctttctt cctttggata atgtagttca tatccattcc ctcttttate	300
t	301

&lt;210&gt; 238

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 238

gggcagggtt tttttttttt ttttttgatg gtgcagaccc ttgctttatt tgtctgactt	60
gttcacagtt cagccccctg ctcaaaaaac caacgggcca gctaaggaga ggaggaggca	120
ccttgagact tccggagtcg aggtcttcca gggttcccca gcccatcaat cattttctgc	180
acccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca	240
gtgtgggacc cagggtctgt ttttcacagt agggagtgga agggatgact aatttcttta	300
t	301

&lt;210&gt; 239

&lt;211&gt; 239

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 239

ataagcagct agggaattct ttatttagta atgtcctaac ataaaagtgc acataactgc	60
ttctgtcaaa ccatgatact gagctttgtg acaaccaga aataactaag agaaggcaaa	120
cataatacct tagagatcaa gaaacattta cacagttcaa ctgtttaaaa atagctcaac	180
attcagccag tgagtagagt gtgaatgccg gcatacacag tatacaggtc cttcaggga	239

&lt;210&gt; 240

<211> 300  
 <212> DNA  
 <213> Homo sapien

<400> 240  
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 gctgggtgag ccagatgact tctgttccct ggtcactttc ttcaatgggg cgaatggggg 180  
 ctgccaggtt tttaaaatca tgcttcatct tgaagcacac ggtcacttca cctcctcac 240  
 gctgtgggtg tactttgatg aaaataccca ctttgttggc ctttctgaag ctataatgtc 300

<210> 241  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 241  
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 ctctccatg tattggaaaa ctgcaaactg gactcaactg gaaggaagtg ctgctgccag 180  
 tgtgaagaac cagcctgagg tgacagaaac ggaagcaaac aggaacagcc agtcttttct 240  
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 g 301

<210> 242  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 242  
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 gtcttcaaga atatatcatt cctttttcac tagaaccat tcaaaatata agtcaagaat 180  
 cttaatatca acaaatatat caagcaaact ggaaggcaga ataactacca taatttagta 240  
 taagtaccca aagttttata aatcaaaagc cctaagtata accattttta gaattcaatc 300  
 a 301

<210> 243  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 243  
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 tgacgtgcag tcggactctg tggcccaagg gtatggctct ctccggcatga tgaccagcgt 180  
 gctggtttgt ccagatggca agacagtaga agcagaggct gccacggga ctgtaaccgg 240  
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 t 301

<210> 244  
 <211> 300  
 <212> DNA  
 <213> Homo sapien

<400> 244  
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ccagggacct tggaaacagt tgacactgta aggtgcttgc tccccaagac acatcctaaa 180  
 aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc ccttcttatt tatgtgaaca 240  
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<210> 245

<211> 301

<212> DNA

<213> Homo sapien

<400> 245

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 tatatactta gataaaaaat gaggtgaatt actatccatt gaaatcatgc tcttagaatt 120  
 aaggccagga gatattgtca ttaatgtara cttcaggaca cttagagtata gcagccctat 180  
 gttttcaaag agcagagatg caattaaata ttgttttagca tcaaaaaggc cactcaatac 240  
 agctaataaa atgaaagacc taatttctaa agcaattcct tataattttac aaagttttaa 300  
 g 301

<210> 246

<211> 301

<212> DNA

<213> Homo sapien

<400> 246

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 agtgcctctt gtgaaaatta aataaaacag ttaattcaaa gccttgatat atgttaccac 180  
 taacaatcat actaaatata ttttgaagta caaagtttga catgctctaa agtgacaacc 240  
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 c 301

<210> 247

<211> 301

<212> DNA

<213> Homo sapien

<400> 247

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 gtgtcctgtg ttcaggtgcg acacacaatc ctcatgggaa caggatcacc catgcgctgc 180  
 ccttgatgat caaggttggg gcttaagtgg attaagggag gcaagttctg ggttccttgc 240  
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 a 301

<210> 248

<211> 301

<212> DNA

<213> Homo sapien

<400> 248

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 acaggaagaa agtggttttg aagacagcca aagaaataaa agcagattaa attgtatcag 180  
 gtacattcca gcctgtttgg aactccataa aaacatttca gattttaatc ccgaatttag 240  
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 c 301

<210> 249

<211> 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 249

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ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgteccgccc      120
ccagggagac acagcagtga ctacagagctg gtcgcacact gtgcctccct cctcaccgcc      180
catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag      240
actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt      300
a                                                                                   301

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&lt;210&gt; 250

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 250

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ggctctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacatttctc      60
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cataagcaca tcagtacttt tctctggctg gaatagtaaa cttaaagtatg gtacatctac      180
ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta      240
caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc      300
a                                                                                   301

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&lt;210&gt; 251

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 251

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gccgaggtcc tacatttggc ccagtttccc cctgcacccct ctccagggcc cctgcctcat      60
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ggcagggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct      180
cattggggtc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccgaa      240
cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatcct      300
c                                                                                   301

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&lt;210&gt; 252

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 252

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gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttgtgg catttcctca      60
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tcattccttt ttcactagga acccattcaa aatataagtc aagaatctta atatcaacaa      180
atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag taccctaaag      240
tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc      300
a                                                                                   301

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&lt;210&gt; 253

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 253

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ttccctaaga agatgttatt ttgttgggtt ttgttccccc tccatctcga ttctcgtacc      60
caactaaaaa aaaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctccttagct      120

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tggtctgatt gttttcagac cttaaaatat aaacttgttt cacaagcttt aatccatgtg	180
gatttttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt	240
tccatagtgc ccacagggtta ttcctcacat tttctccata ggaaaatgct ttttccaag	300
g	301

&lt;210&gt; 254

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 254

cgctgcgcct ttcccttggg ggaggggcaa ggccagaggg ggtccaagtg cagcacgagg	60
aacttgacca attcccttga agcgggtggg ttaaaccctg taaatgggaa caaaatcccc	120
ccaaatctct tcatcttacc ctggtggact cctgactgta gaattttttg gttgaaacaa	180
gaaaaaata aagcttttga cttttcaagg ttgcttaaca ggtactgaaa gactggcctc	240
acttaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgc	300
t	301

&lt;210&gt; 255

&lt;211&gt; 302

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 255

agcttttttt tttttttttt tttttttttt ttcattaaaa aatagtgtct tttattataa	60
attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat	120
tgggattttg ttgagttctt caagcatctc ctaataccct caagggcctg agtagggggg	180
aggaaaaagg actggaggtg gaatctttat aaaaaacaag agtgattgag gcagattgta	240
aacattatta aaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac	300
aa	302

&lt;210&gt; 256

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 256

gttccagaaa acattgaagg tggcttccca aagtctaact agggatcccc cctctagcct	60
aggaccctcc tccccacacc tcaatccacc aaaccatcca taatgcaccc agataggccc	120
acccccaaaa gcttgagcac cttgagcaca cagttatgac caggacagac tcatctctat	180
aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggaagtgt	240
gtggcctctc ggctgggta gcaagaacat tcagggtagg cctaagttn tcgtgttagt	300
t	301

&lt;210&gt; 257

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 257

gttgtggagg aactctggct tgetcattaa gtectactga ttttactat cccctgaall	60
tccccactta tttttgtctt tcaactatgc aggccttaga agaggtctac ctgcctccag	120
tcttacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat	180

gtcacattac tcccttcagt gattttcttgt agaagtgcc atccctgaat gccaccaaga 240  
 tcttaattctt cacatcttta atcttatctc tttgactcct ctttacaccg gagaaggctc 300  
 c 301

<210> 258  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (301)  
 <223> n = A,T,C or G

<400> 258  
 cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc 60  
 aggggccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc 120  
 cccagggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat cttaacactg 180  
 atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtgggtgcat 240  
 tggatgccc tgggagcgcc ggtggagtaa cgttgggtcca tggaaagcag cgcccacaac 300  
 t 301

<210> 259  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (301)  
 <223> n = A,T,C or G

<400> 259  
 tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg 60  
 gtgtcctgaa gtgatttggg cccctgaggg cagacaccta agtaggaatc ccagtgggaa 120  
 gcaaagccat aaggaagccc aggattcctt gtgatcagga agtgggcccag gaaggctctgt 180  
 tccagctcac atctcatctg catgcagcac ggaccggatg cgcccactgg gtcttggett 240  
 ccctcccac tctcaagca gtgtccttgt tgagccattt gcatccttgg ctccagggtg 300  
 c 301

<210> 260  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 260  
 ttttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaa at aagcaatgg 60  
 aaggtgtctt aacttgaaaa agattaggag tcactggttt acaagttata attgaatgaa 120  
 agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaacia caggattaac 180  
 tagggcaaaa taataaagtg tgtggaagcc ctgataagt cttaataaac agactgattc 240  
 actgagacat cagtacctgc ccgggcggcc gctcgagccg aattctgcag atatccatca 300  
 c 301

<210> 261  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

&lt;400&gt; 261

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aatatttoga gcaaactctg taactaatgt gtctccataa aaggctttga actcagtga 60
tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggt 120
agcaccaact attccataga attcatcagc aggaaataaa ggctcttcag aagggttcaat 180
ggtgacatcc aatttcttct gataatttag attcctcaca accttcctag ttaagtgaag 240
ggcatgatga tcatccaaag cccagtgggc acttactcca gactttctgc aatgaagatc 300
a 301

```

&lt;210&gt; 262

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 262

```

gaggagagcc tgttacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc 60
tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaaacc ctgagtcacc 120
cctagacttc ctaaaccaga tctctggtgg ctggaacctg gcactctgca tttgtaatga 180
gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgcgc 240
catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat 300
c 301

```

&lt;210&gt; 263

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 263

```

tttagcttgt ggtaaagtac tcacaaaact gatttttaaaa tcaagttaat gtgaattttg 60
aaaattacta cttaatccta attcacaata acaatggcat taagggtttga cttgagttgg 120
ttcttagtat tatttatggg aaataggctc ttaccacttg caaataactg gccacatcat 180
taatgactga cttcccagta aggctctcta aggggtaagt angaggatcc acaggatttg 240
agatgctaag gccccagaga tcgtttgatc caaccctctt attttcagag gggaaaatgg 300
g 301

```

&lt;210&gt; 264

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 264

```

aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc 60
aatgaatgac tctaaaaaca atatttacat ttaatgggtt gtagacaata aaaaaacaag 120
gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaag 180
ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 240
acccttcata taaattcact atcttggctt gaggcactcc ataaaatgta tcacgtgcac 300
a 301

```

&lt;210&gt; 265

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 265



tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcattcttgt 60  
 cttcttgga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta 120  
 catattcttg gaagtctcta atcaactttt gttccatttg tttcatttct tcaggaggga 180  
 ttttcagttt gtcaacatgt tctctaacaa cacttgccca tttctgtaaa gaatccaaag 240  
 cagtcgaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg 300  
 c 301

<210> 266  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 266  
 tacogtctgc ctttcctccc atccaggcca tctgogaatc tacatgggtc ctccattctg 60  
 acaccagatc actcttttct ctaccacacag gcttgctatg agcaagagac acaacctcct 120  
 ctctctctgtg ttccagcttc ttttctgtgt ctcccccccc cttaagttct attcctgggg 180  
 atagagacac caatacccat aacctctctc ctaagcctcc ttataacca ggggtgcacag 240  
 cacagactcc tgacaactgg taaggccaat gaactgggag ctacacagctg gctgtgcctg 300  
 a 301

<210> 267  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 267  
 aaagagcaca ggccagctca gctgcccctg gccatctaga ctacgcctgg ctccatgggg 60  
 gttctcagtg ctgagtcctat ccaggaaaag ctacacctaga cttcttgagg ctgaatcttc 120  
 atcctcacag gcagcttctg agagcctgat attcctagcc ttgatgggtc ggagtaaage 180  
 ctcatctga ttctctctct tcttttcttt caagttggct ttctctacat cctctgttc 240  
 aattcgttc agcttgtctg ctttagccct catttccaga agcttcttct ctttggcatc 300  
 t 301

<210> 268  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 268  
 aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctgggagt tttcttctta 60  
 gatcttgga gagctgggtc ttctaaggag aaggaggaag gacagatgta actttggatc 120  
 tcgaagagga agtctaattg aagtaattag tcaacgggtc ttgttttagac tcttggaata 180  
 tgctgggtgg ctacgtgagc ccttttgagg aaagcaagta ttattcttaa ggagtaacca 240  
 cttccattg ttctactttc taccatcatc aattgtatat tatgtattct ttggagaact 300  
 a 301

<210> 269  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 269  
 taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat 60  
 aaaattacct ttattcacac atctcaaac aattctgcaa attcttagtg aagtttaact 120  
 atagtcacag accttaata ttacacattg tttctatgtc tactgaaaat aagttcacta 180  
 cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca cccccaatta 240  
 tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc 300  
 t 301

<210> 270  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 270  
 cattgaagag cttttgcgaa acatcagaac acaagtgcctt ataaaattaa ttaagcctta 60  
 cacaagaata catattcctt ttattttctaa ggagttaaac atagatgtag ctgatgtgga 120  
 gagcttgctg gtgcagtgca tattggataa cactattcat ggccgaattg atcaagtcaa 180  
 ccaactcctt gaactggatc atcagaagaa ggggtggtgca cgatatactg cactagataa 240  
 tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggcctt aacagaaaac 300  
 a 301

<210> 271  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 271  
 aaaaggttct cataagatta acaattttaa taaatatttg atagaacatt ctttctcatt 60  
 tttatagctc atcttttaggg ttgatattca gttcatgctt cccttgctgt tcttgatcca 120  
 gaattgcaat cacttcatca gcctgtattc gctccaattc tctataaagt ggggtccaagg 180  
 tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt 240  
 tctctcctcc agatganaac tgatcatgcg cccacatttt gggttttata gaagcagtca 300  
 c 301

<210> 272  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 272  
 taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaagtgc 60  
 ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120  
 tccaataatt ccctcatgat gagcaagaaa aattctttgc gcacccctcc tgcattccaca 180  
 gcatcttctc caacaaatat aaccttgagt ggcttcttgc aatctatggt ctttggtttc 240  
 ctaaggactt ccattgcac cctacaata ttttctctac gcaccactag aattaagcag 300  
 g 301

<210> 273  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 273  
 acatgtgtgt atgtgtatct ttgggaaaan aanaagacat cttgtttayt atttttttgg 60  
 agagangctg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactyga 120

```

gaaccgtcta aaaataaaat ttaccatgtc dtatattcct tatagtatgc ttatttcacc      180
ttytttctgt ccagagagag tatcagtgac ananatttma ggggtgaamac atgmattggg      240
gggacttnty ttacngagm accctgcccg sgcgccctcg makcngantt ccgcsananc      300
t                                                                           301

```

&lt;210&gt; 274

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 274

```

cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg      60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa      120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttggt gaaaagtcca      180
tctaggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc      240
aattgtgctt cttttgataa gaagctttctt tggtcatatc aggaaattcc aganaaagtc      300
c                                                                           301

```

&lt;210&gt; 275

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 275

```

tcgggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg      60
gggtgaaatt ggccaacttt ctattaactt atgttggtgca ttttgccacc aacagtaagc      120
tggtcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtgagg      180
tcaagagact cccaggcctc agcgtacctg cccgggcggc cgctcgaagc cgaattctgc      240
agatatccat cacactggcg gncgctcgan catgcatcta gaaggnccaa ttcgccttat      300
a                                                                           301

```

&lt;210&gt; 276

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 276

```

tgtacacata ctcaataaat aatgactgc attgtgggtat tattactata ctgattatat      60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat      120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc      180
caatacatTT aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt      240
aaaactattc agtatgtttc cettgcttca tgtctgagaa ggctctcctt caatggggat      300
g                                                                           301

```

&lt;210&gt; 277

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 277  
 ttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag 60  
 atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg 120  
 gaatcatggc actcctgata ctttcccaaa tcaacactct caatgcccc aacctgctct 180  
 caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga 240  
 gttcncctgc gattacatct gaccagtctc ctttttccga agtcctccg ttcaatcttg 300  
 c 301

<210> 278  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 278  
 taccactaca cttcagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60  
 aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgta 120  
 cagtctctac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgcc 180  
 aatgaacatc tcatgtgtgc tcacaatggt ctggcactat tataagtgtc tcacagggtt 240  
 tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300  
 c 301

<210> 279  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 279  
 aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60  
 gttatattaa ttgccaatat aagtaaataat agattatata tgtatagtgt ttcacaaagc 120  
 ttagaccttt acctccagc caccacacag tgcttgatat ttcagagtca gtcattgggt 180  
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240  
 catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300  
 a 301

<210> 280  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 280  
 ggtactggag ttttctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg 60  
 tagaaagggt gtggaaccaa attgtggtca atggaaatag gagaatatgg ttctcactct 120

tgagaaaaaa acctaagatt agcccaggta gttgcctgta acttcagttt ttctgcctgg 180  
 gtttgatata gtttaggggtt ggggttagat taagatctaa attacatcag gacaaagaga 240  
 cagactatta actccacagt taattaagga ggtatgttcc atgtttattt gttaaagcag 300  
 t 301

<210> 281  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 281  
 aggtacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttggatatcc 60  
 gccgagcaat ccaaatcctg aatgaagggtt catcttctga aaaaggagat ctgaatctca 120  
 atgtggtagc aatggcttta tcgggttata cggatgagaa gaactccctt tggagagaaa 180  
 tgtgtagcac actgcgatta cagctaaata acccgatttt gtgtgtcatg ttgcatcttc 240  
 tgacaagtga aacaggatct tacgatggag ttttgtatga aaacaaagtt gcagtacctc 300  
 g 301

<210> 282  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 282  
 caggtactac agaattaaaa tactgacaag caagtagttt cttggcgtgc acgaattgca 60  
 tccagaaccc aaaaattaag aaattcaaaa agacattttg tgggcacctg ctagcacaga 120  
 agcgcagaag caaagcccag gcagaacctt gctaacctta cagctcagcc tgcacagaag 180  
 cgcagaagca aagcccaggc agaaccatgc taaccttaca gctcagcctg cacagaagcg 240  
 cagaagcaaa gccccaggcag aacatgctaa ccttacagct cagcctgcac agaagcacag 300  
 a 301

<210> 283  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 283  
 atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaaag gatgcaaaag 60  
 cactttgagg gctttataat aatatgctgc ttgaaaaaaa aaatgtgtag ttgatactca 120  
 gtgcatctcc agacatagta aggggttgct ctgaccaatc aggtgatcat tttttctatc 180  
 acttcccagg ttttatgcaa aaattttggt aaattctata atggtgatat gcattcttta 240  
 ggaaacatat acatttttta aaatctattt tatgtaagaa ctgacagacg aatttgcttt 300  
 g 301

<210> 284  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 284  
 caggtacaaa acgctattaa gtggcttaga attgaacat ttgtggtctt tatttacttt 60  
 gcttcgtgtg tgggcaaagc aacatcttcc ctaaaatat attaccaaga aaagcaagaa 120  
 gcagattagg tttttgacaa aacaaacagg ccaaaagggg gctgacctgg agcagagcat 180  
 ggtgagaggc aaggcatgag agggcaagtt tgttgtggac agatctgtgc ctactttatt 240  
 actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaatt 300  
 a 301

<210> 285

<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 285  
acatcaccat gatcggatcc cccacccatt atacgttgta tgtttacata aatactcttc 60  
aatgatcatt agtgttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac 120  
caggaaagca aatgctatct acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180  
attaaatatg tctgacttct tttgaggtea cactgactagg caaatgctat ttacgatctg 240  
caaaagctgt ttgaagagtc aaagcccca tgtgaacacg atttctggac cctgtaacag 300  
t 301

<210> 286  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 286  
taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct 60  
tgtatattat ttttgcccta cagtggatca ttctagtagg aaaggacagt aagatttttt 120  
atcaaaatgt gtcagccag taagagatgt tatattcttt tctcatttct tccccacca 180  
aaaataagct accatatagc ttataagtct caaatttttg ccttttacta aaatgtgatt 240  
gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt tttcccttg 300  
t 301

<210> 287  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 287  
tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg 60  
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggg tagaaatatg 120  
aaatgatttg gttatgaacg cacagttag gcagcagggc cagaatcctg accctctgcc 180  
cgtggttat ctctcccca gcttggtgc ctcagtgtat cacagtatc cattttgttt 240  
gttgcagtgc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc 300  
t 301

<210> 288  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 288  
gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60  
agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa 120  
gatctttaa gacaatttca agagaatatt tctttaaagt tggcaatttg gagatcatac 180  
aaaagcatct gcttttgtga ttttaatttag ctcactctgg cactggaaga atccaaacag 240  
cttgccctaa ttttgatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300  
a 301

<210> 289  
<211> 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 289

```

ggtagactgt ttccatgtta tgtttctaca cattgctacc tcagtgtcc tggaaactta      60
gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatcttg      120
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa      180
cgttctataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aagagaaaga      240
tgtgtttgt tttggactct ctgtgggtccc ttccaatgct gtgggtttcc aaccagnnga      300
a

```

&lt;210&gt; 290

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 290

```

aactgagct cttcttgata aatatacaga atgcttgga tatacaagat tctatactac      60
tgactgatct gttcatttct ctccagctc ttaccccaa aagcttttcc accctaagtg      120
ttctgacctc cttttctaata cacagtaggg atagaggcag anccacctac aatgaacatg      180
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctagcagtgc      240
tgccctgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtgc      300
a

```

&lt;210&gt; 291

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 291

```

caggtacca tttcttctat cctagaacaa tttcatttta tgttgttgaa acataacaac      60
tatatcagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc      120
tttactcttt tgtttatagg tgaatcacia aatgtatttt tatgtattct gtagttcaat      180
agccatggct gtttacttca ttttaatttat ttagcataaa gacattatga aaaggcctaa      240
acatgagctt cacttcccca ctaactaatt agcatctgtt atttcttaac cgtaatgcct      300
a

```

&lt;210&gt; 292

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 292

```

accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc      60
tgtattaaat aatttttaag tttaaaagat aaaataccat cattttaaat gttggtattc      120
aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg      180
ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc      240
tcactacaca cacagacccc acagtcctat atgccacaaa cacatttcca taacttgaaa      300
a                                                                                   301

```

<210> 293  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

```

<400> 293
ggtaccaaagt gctgggtgcca gcctgttacc tgttctcact gaaaagtctg gctaagtctc      60
ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactggt      120
aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt      180
gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg      240
ccgcgaccac gctaagccga attctgcaga tatccatcac actggcgggc gctcgagcat      300
g                                                                                   301

```

<210> 294  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

```

<400> 294
tgacccataa caatatacac tagctatctt tttaaactgtc catcattagc accaatgaag      60
attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag      120
tttaactata gtcacaganc ttaaattatc acattgtttt ctatgtctac tgaaaataag      180
ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc      240
cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt      300
t                                                                                   301

```

<210> 295  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

```

<400> 295
gtactctttc tctcccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta      60
cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac      120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccactctctga      180
actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggtga attggatggg      240
tctcagaacc atttcaccca gacagcctgt ttctatcctg ttaataaat tagtttgggt      300
tctct                                                                                   305

```

<210> 296  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

```

<400> 296
aggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct      60

```



```

cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg      120
attaatataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac      180
tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt      240
tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg      300
c                                                                           301

```

&lt;210&gt; 297

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (300)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 297

```

actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttggtgcta      60
aaggttttga aaaccttgaa ggagaatcat ttgacaaga agtacttaag agtctagaga      120
acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt      180
tccatcattg ggagtgcact ggccatccct caaaatttgt ctgggctggc ctgagtggtc      240
accgcacctc ggccgcgacc acgctaagcc gaattctgca gatatccatc aactggcgcg      300

```

&lt;210&gt; 298

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 298

```

tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc cctcccgcg      60
ggcatctgag agacctgggtg ttccagtgtt tctggaaatg ggtcccagtg ccgccggctg      120
tgaagctctc agatcaatca cgggaagggc ctggcggtgg tggccacctg gaaccacct      180
gtcctgtctg ttacatttc actaycaggt tttctctggg cattacnatt tgttccccta      240
caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcagggtggc ctcagcgagg      300
t                                                                           301

```

&lt;210&gt; 299

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 299

```

gttttgagac ggagtttcac tctgttgcc cagactggac tgcaatggca gggctctctgc      60
tcaactgcacc ctctgcctcc caggttcgag caattctcct gcctcagcct cccaggtagc      120
tggtattgca ggctcagcc accataccca gctaattttt ttgtattttt agtagagacg      180
gagtttcgcc atgttgccca gctgggtctca aactcctgac ctcaagcgac ctgcctgcct      240
cggcctccca aagtgtgga attataggca tgagtcaaca cgcccagcct aaagatattt      300
t                                                                           301

```

&lt;210&gt; 300

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 300

attcagtttt atttgcctgcc ccagttatctg taaccaggag tgccacaaaa tcttgccaga	60
tatgtccac acccactggg aaaggtccc acctggctac ttcctctatc agctgggtca	120
gctgcattcc acaaggttct cagcctaag agtttacta cctgccagtc tcaaaactta	180
gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttggtac	240
tataaagcct gcctctaaca gtcttgctt cttcacacca atcccgagcg catccccat	300
g	301

&lt;210&gt; 301

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 301

ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc	60
agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt	120
gggaactcac aaagaccctc agagctgaga caccacacaac agtgggagct cacaagacc	180
ctcagagctg agacacccac aacagtggga gtcacaaaag accctcagag ctgagacacc	240
cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt	300
t	301

&lt;210&gt; 302

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 302

aggtacacat ttagcttggt gtaaattgact cacaaaaactg attttaaaat caagttaatg	60
tgaattttga aaattactac ttaattctaa ttcacaataa caatggcatt aaggtttgac	120
ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg	180
ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca	240
caggatttga gatgctaagg cccagagat cgtttgatcc aaccctctta ttttcagagg	300
g	301

&lt;210&gt; 303

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 303

aggtaccaac tgtggaaata ggtagaggat cttttttct tccatatca actaagttgt	60
atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac	120
tggtcaatgg aactaccgct tgcatgttaa aaatgggtgt ttgtgaaatg atcataggcc	180
agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc	240
catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac	300
c	301

&lt;210&gt; 304

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 304

acatggatgt tattttgcag actgtcaacc tgaatttgta tttgcttgac attgccta	60
tattagtttc agtttcagct taccactttt ttgtctgcaa catgcaraas agacagtgcc	120
cttttttagtg tatcatatca ggaatcatct cacattgggt tgtgccatta ctggtgcagt	180
gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga	240

ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct 300  
c 301

<210> 305

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 305

gangtacagc gtgggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag 60  
caggggggaca gacctggaca gacacgttgt catttgcctgc tgtgggtagg aaaatgggag 120  
taaaggagga gaaacagata caaaatctcc aactcagtat taaggatttc tcatgcctag 180  
aatattggta gaaacaagaa tacattcata tggcaaataa ctaacatgg tggaacaaaa 240  
ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag 300  
a 301

<210> 306

<211> 8

<212> PRT

<213> Homo sapien

<400> 306

Val Leu Gly Trp Val Ala Glu Leu  
1 5

<210> 307

<211> 637

<212> DNA

<213> Homo sapien

<400> 307

acagggratg aagggaaagg gagaggatga ggaagccccc ctggggattt ggtttggtcc 60  
ttgtgatcag gtgggtctatg gggcttatcc ctacaaagaa gaatccagaa ataggggac 120  
attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt 180  
cacaccattg gtgaggagg gattaccacc ctggggttat gaagatggtt gaacacccca 240  
cacatagcac cggagatatg agatcaacag tttcttagcc atagagattc acagcccaga 300  
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg 360  
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacggtgagg caaactctga 420  
tttcctgggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtga 480  
actcattagg ctgagaacct tgtggaatgc acttgacca sctgatagag gaagtagcca 540  
gggtgggagcc tttcccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg 600  
ttacagatac tggggcagca aataaaactg aatcttg 637

<210> 308

<211> 647

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(647)

<223> n = A,T,C or G

&lt;400&gt; 308

acgattttca	ttatcatgta	aatcgggtca	ctcaaggggc	caaccacagc	tgggagccac	60
tgctcagggg	aaggttcata	tgggactttc	tactgcccac	ggttctatac	aggatataaa	120
ggngcctcac	agtatagatc	tggtagcaaa	gaagaagaaa	caaacactga	tctctttctg	180
ccacccctct	gaccctttgg	aactcctctg	accctttaga	acaagcctac	ctaatactctg	240
ctagagaaaa	gaccaacaac	ggcctcaaag	gatctcttac	catgaaggtc	tcagctaatt	300
cttggttaag	atgtgggttc	cacattaggt	tctgaatatg	gggggaaggg	tcaatttgct	360
cattttgtgt	gtggataaag	tcaggatgcc	caggggccag	agcagggggc	tgcttgcttt	420
gggaacaatg	gctgagcata	taaccatagg	ttatggggaa	caaaacaaca	tcaaagtcac	480
tgtatcaatt	gcatgaaga	cttgagggac	ctgaatctac	cgattcatct	taaggcagca	540
ggaccagttt	gagtggaac	aatgcagcag	cagaatcaat	ggaaacaaca	gaatgattgc	600
aatgtccttt	ttttctcct	gcttctgact	tgataaaagg	ggaccgt		647

&lt;210&gt; 309

&lt;211&gt; 460

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 309

actttatagt	ttaggctgga	cattggaaaa	aaaaaaaaagc	cagaacaaca	tgtgatagat	60
aatatgattg	gctgcacact	tccagactga	tgaatgatga	acgtgatgga	ctattgtatg	120
gagcacatct	tcagcaagag	ggggaaatac	tcatcatttt	tggccagcag	ttgtttgatc	180
accaaacatc	atgccagaat	actcagcaaa	ccttcttagc	tcttgagaag	tcaaagtccg	240
ggggaattta	ttcctggcaa	ttttaattgg	actccttatg	tgagagcagc	ggctaccacg	300
ctgggggtgt	ggagcgaacc	cgtcactagt	ggacatgcag	tggcagagct	cctggttaac	360
acctagagga	atacacaggc	acatgtgtga	tgccaagcgt	gacacctgta	gcactcaaat	420
ttgtcttggt	tttgtctttc	ggtgtgtaag	attcttaagt			460

&lt;210&gt; 310

&lt;211&gt; 539

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 310

acgggactta	tcaaataaag	ataggaaaag	aagaaaactc	aaatattata	ggcagaaatg	60
ctaaaggttt	taaaatatgt	caggattgga	agaaggcatg	gataaagaac	aaagtccagt	120
taggaaagag	aaacacagaa	ggaagagaca	caataaaagt	cattatgtat	tctgtgagaa	180
gtcagacagt	aagatttgtg	ggaaatgggt	tggtttgttg	tatggatgtg	atttttagcaa	240
taatctttat	ggcagagaaa	gctaaaatcc	tttagcttgc	gtgaatgata	acttgctgaa	300
ttcctcaagg	taggcatgat	gaaggagggt	ttagaggaga	cacagacaca	atgaactgac	360
ctagatagaa	agccttagta	tactcagcta	ggaatagtga	ttctgagggc	acactgtgac	420
atgattatgt	cattacatgt	atggtagtga	tggggatgat	aggaaggaag	aacttatggc	480
atattttcac	ccccacaaaa	gtcagttaaa	tattgggaca	ctaaccatcc	aggtcaaga	539

&lt;210&gt; 311

&lt;211&gt; 526

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (526)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 311

caaatttgag	ccaatgacat	agaattttac	aaatcaagaa	gcttattctg	gggccatttc	60
ttttgacgtt	ttctctaaac	tactaaagag	gcattaatga	tccataaatt	atattatcta	120
catttacagc	attttaaagt	tggtcagcat	gaaatattag	ctacagggga	agctaaataa	180

atataacatg gaataaagat ttgtccttaa atataatcta caagaagact ttgatatttg 240  
tttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa 300  
aaaatgggga aactctgaag gggtttaagt atcttacctg aagctacaga ctccataacc 360  
tctctttaca gggagctcct gcagccccta cagaaatgag tggctgagat tcttgattgc 420  
acagcaagag cttctcatct aaacccttct cctttttagt atctgtgtat caagtataaa 480  
agttctataa actgtagtnt acttatttta atcccaaaag cacagt 526

<210> 312

<211> 500

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (500)

<223> n = A,T,C or G

<400> 312

cctctctctc cccaccccct gactctagag aactgggttt tctcccagta ctccagcaat 60  
tcattttctga aagcagttga gccactttat tccaaagta actgcagatg ttcaaactct 120  
ccattttctct ttccttcca cctgccagtt ttgtcgactc tcaacttgct atgagtgtaa 180  
gcatlaagga cattatgctt cttcgattct gaagacaggc cctgctcatg gatgactctg 240  
gcttcttagg aaaatatttt tcttccaaa tcagtaggaa atctaaactt atcccctctt 300  
tgcagatgct tagcagcttc agacatttgg ttaagaacct atgggaaaaa aaaaaatcct 360  
tgctaagtgt gtttcccttg taaaccanga ttcttatttg nctggtatag aatatcagct 420  
ctgaacgtgt ggtaagatt tttgtgtttg aatataggag aaatcagttt gctgaaaagt 480  
tagtcttaat tatctattgg 500

<210> 313

<211> 718

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (718)

<223> n = A,T,C or G

<400> 313

ggagatttgt gtggtttgca gccgaggag accaggaaga tctgcatggt gggaaggacc 60  
tgatgataca gaggtgagaa ataagaaagg ctgctgactt taccatctga ggccacacat 120  
ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa 180  
gtagtgacat gtttttgca atttccagcc cttttaaata tccacacaca caggaagcac 240  
aaaaggaagc acagagatcc ctgggagaaa tgcccggccg ccatcttggg tcatcgatga 300  
gcctcgccct gtgcctgntc ccgcttgatg ggaaggaca ttagaaaatg aattgatgtg 360  
ttccttaag gatggcagga aaacagatcc tgggtgtgat atttatttga acgggattac 420  
agatttgaaa tgaagtcaca aagtgcagat taccaatgag aggaacacag acgagaaaat 480  
cttgatggtt cacaagacat gcaacaaaca aaatggaata ctgtgatgac acgagcagcc 540  
aactggggag gagataccac ggggcagagg tcaggattct ggccctgctg cctaactgtg 600  
cgttatacca atcatttcta tttctaccct caaacaagct gtngaataac tgacttacgg 660  
ttctnttggc ccacatttct atnatccacc cntcntttt aannttanc caaantgt 718

<210> 314

<211> 358

<212> DNA

<213> Homo sapien

<400> 314

gtttattttac attacagaaa aaacatcaag acaatgtata ctatttcaaa tatatccata 60  
 cataatcaaa tatagctgta gtacatgttt tcattggtgt agattaccac aaatgcaagg 120  
 caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg tgtagtccaa 180  
 gctctcggta gtccagccac tgtgaaacat gctcccttta gattaacctc gtggacgctc 240  
 ttgttgattt gctgaactgt agtgccctgt attttgcttc tgtctgtgaa ttctgttget 300  
 tctggggcat ttccttggtga tgcagaggac caccacacag atgacagcaa tctgaatt 358

<210> 315

<211> 341

<212> DNA

<213> Homo sapien

<400> 315

taccacctcc ccgctggcac tgatgagccg catcaccatg gtcaccagca ccatgaaggc 60  
 ataggtgatg atgaggacat ggaatgggccc cccaaggatg gtctgtccaa agaagcgagt 120  
 gacccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag ccccaatgac 180  
 agtcaccagc tccccagcca gccggatata gtccttaggg gtcatgtagg ctctctgaag 240  
 tagcttctgc tgtaagaggg tgttgccccg ggggctcgtg cggttattgg tctgggctt 300  
 gagggggcgg tagatgcagc acatgggtgaa gcagatgatg t 341

<210> 316

<211> 151

<212> DNA

<213> Homo sapien

<400> 316

agactgggca agactcttac gccccacact gcaatttggt cttgttgccg tatccattta 60  
 tgtgggcctt tctcgagttt ctgattataa acaccactgg agcgatgtgt tgactggact 120  
 cattcagggg gctctggttg caatattagt t 151

<210> 317

<211> 151

<212> DNA

<213> Homo sapien

<400> 317

agaactagt gatacctaag aaataacctga aacatatatt ggcatattatc aatggctcaa 60  
 atcttcattt atctctggcc ttaaccctgg ctctgagggc tgcggccagc agatcccagg 120  
 ccagggctct gttcttgcca cactgcttg a 151

<210> 318

<211> 151

<212> DNA

<213> Homo sapien

<400> 318

actggtggga ggcgctgttt agttggctgt tttcagaggg gtcttttcgga gggacctcct 60  
 gctgcaggct ggagtgtctt tattcttggc gggagaccgc acattccact gctgaggctg 120  
 tgggggcggg ttatcaggca gtgataaaca t 151

<210> 319

<211> 151

<212> DNA

<213> Homo sapien

<400> 319

aactagtga tccagagcta taggtacagt gtgatctcag ctttgcaaac acattttcta 60  
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taagattggg tttatgtgat tttagtgggt a 151

<210> 320  
<211> 150  
<212> DNA  
<213> Homo sapien

<400> 320  
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gagcggtgc cctttttttt tttttttttg ggggggaatt tttttttttt aatagttatt 120  
gagtgttcta cagcttacag taaataccat 150

<210> 321  
<211> 151  
<212> DNA  
<213> Homo sapien

<400> 321  
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taggttgga ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg 120  
tgctctgag aaatcaaagt cttcatacac t 151

<210> 322  
<211> 151  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(151)  
<223> n = A,T,C or G

<400> 322  
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tttgggttg gtcagtttg cacagggtt ggagatggtg acagtcttct ggcattcggc 120  
attgtgcagg gctcgttca nacttccagt t 151

<210> 323  
<211> 151  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(151)  
<223> n = A,T,C or G

<400> 323  
tgaggacttg tktttttttt ctttatattt aatcctctta ckttgtaa atattgccta 60  
nagactcant tactaccag tttgtggtt twtgggagaa atgtaactgg acagttagct 120  
gttcaatyaa aaagacactt ancccatgtg g 151

<210> 324  
<211> 461  
<212> DNA  
<213> Homo sapien

<220>

<221> misc\_feature  
<222> (1)...(461)  
<223> n = A,T,C or G

<400> 324

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agaagtgggc agctaaagga atccagggtg ttgggtggac tgtaataacc tttgatgaaa	120
agagttacta cgaatcccat cttggttcca gctatatcac tgacagcatg gtagaagact	180
gcgaacctca cttctagact ttcacgggtg gacgaaacgg gttcagaaac tgccaggggc	240
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cacacaaatg caatagtggg tcaactgcatt ttacactgaa ccaaagctaa acccggtgtt	360
gccaccatgc accatggcat gccagagttc aacactgttg ctcttgaaaa ttgggtctga	420
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<210> 325  
<211> 400  
<212> DNA  
<213> Homo sapien

<400> 325

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agtaagagtg gtggcctatt tcagctgctt tgacaaaatg actggctcct gacttaacgt	180
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gttttgtttt ggactctctg tggctccctc caatgctgtg ggtttccaac caggggaagg	300
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<210> 326  
<211> 1215  
<212> DNA  
<213> Homo sapien

<400> 326

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acagtgcctc cttgtggcac gttgaccaa ccttaccagt tggtttttca tttttgtcc	1140
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aaaaaaaaaa aaaaa	1215

<210> 327  
<211> 220



&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 327

Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met  
 1 5 10 15  
 Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val  
 20 25 30  
 Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly  
 35 40 45  
 Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu  
 50 55 60  
 Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala  
 65 70 75 80  
 Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp  
 85 90 95  
 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn  
 100 105 110  
 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro  
 115 120 125  
 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys  
 130 135 140  
 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly  
 145 150 155 160  
 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro  
 165 170 175  
 Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala  
 180 185 190  
 Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys  
 195 200 205  
 Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 210 215 220

&lt;210&gt; 328

&lt;211&gt; 234

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 328

cgctcgtctc tggtagctgc agccaaatca taaacggcga ggactgcagc ccgcactcgc 60  
 agccctggca ggccggcactg gtcattggaaa acgaattggt ctgctcgggc gtccctgggtgc 120  
 atccgcagtg ggtgctgtca gccacacact gtttccagaa ctctacacc atcgggctgg 180  
 gcctgcacag tcttgaggcc gaccaagagc caggagacca gatggtggag gcca 234

&lt;210&gt; 329

&lt;211&gt; 77

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 329

Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly Glu Asp Cys Ser  
 1 5 10 15  
 Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu  
 20 25 30  
 Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr  
 35 40 45  
 His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu  
 50 55 60

Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala  
 65 70 75

<210> 330  
 <211> 70  
 <212> DNA  
 <213> Homo sapien

<400> 330

cccaacacaa tggcccgatc ccatccctga ctccgccctc aggatcgctc gtctctggta 60  
 gctgcagcca 70

<210> 331  
 <211> 22  
 <212> PRT  
 <213> Homo sapien

<400> 331

Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu  
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 Val Ser Gly Ser Cys Ser  
 20

<210> 332  
 <211> 2507  
 <212> DNA  
 <213> Homo sapien

<400> 332

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aaaaaaaaaa	aaaaatccta	aaaacaaaca	aacaaaaaaa	acaattcttc	attcagaaaa	1980
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&lt;210&gt; 333

&lt;211&gt; 3030

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 333

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&lt;210&gt; 334

&lt;211&gt; 2417

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 334

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<212> DNA

<213> Homo sapien

<400> 335

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 <211> 147  
 <212> PRT  
 <213> Homo sapien

<400> 336  
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 Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln  
 35 40 45  
 Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala  
 50 55 60  
 Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln  
 65 70 75 80  
 Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln  
 85 90 95  
 Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala  
 100 105 110  
 Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn  
 115 120 125  
 Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro  
 130 135 140  
 Ala Phe Trp  
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<210> 337  
 <211> 9  
 <212> PRT  
 <213> Homo sapien

<400> 337  
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<210> 338  
 <211> 9  
 <212> PRT  
 <213> Homo sapien

<400> 338  
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 1 5

<210> 339  
 <211> 318  
 <212> PRT  
 <213> Homo sapien

<400> 339  
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 Cys Thr Ser Thr Val Gln Leu Pro Gly Lys Val Val Val Val Thr Gly  
 35 40 45  
 Ala Asn Thr Gly Ile Gly Lys Glu Thr Ala Lys Glu Leu Ala Gln Arg  
 50 55 60  
 Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu  
 65 70 75 80  
 Val Ala Lys Glu Ile Gln Thr Thr Thr Gly Asn Gln Gln Val Leu Val  
 85 90 95  
 Arg Lys Leu Asp Leu Ser Asp Thr Lys Ser Ile Arg Ala Phe Ala Lys  
 100 105 110  
 Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala  
 115 120 125  
 Gly Val Met Met Cys Pro Tyr Ser Lys Thr Ala Asp Gly Phe Glu Met  
 130 135 140  
 His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu  
 145 150 155 160  
 Leu Glu Lys Leu Lys Glu Ser Ala Pro Ser Arg Ile Val Asn Val Ser  
 165 170 175  
 Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly  
 180 185 190  
 Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala  
 195 200 205  
 Asn Ile Leu Phe Thr Gln Glu Leu Ala Arg Arg Leu Lys Gly Ser Gly  
 210 215 220  
 Val Thr Thr Tyr Ser Val His Pro Gly Thr Val Gln Ser Glu Leu Val  
 225 230 235 240  
 Arg His Ser Ser Phe Met Arg Trp Met Trp Trp Leu Phe Ser Phe Phe  
 245 250 255  
 Ile Lys Thr Pro Gln Gln Gly Ala Gln Thr Ser Leu His Cys Ala Leu  
 260 265 270  
 Thr Glu Gly Leu Glu Ile Leu Ser Gly Asn His Phe Ser Asp Cys His  
 275 280 285  
 Val Ala Trp Val Ser Ala Gln Ala Arg Asn Glu Thr Ile Ala Arg Arg  
 290 295 300  
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&lt;210&gt; 340

&lt;211&gt; 483

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 340

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 ctg 483

&lt;210&gt; 341

&lt;211&gt; 344

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 341

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gctgccttac aagtattaaa tattttactt ctttccataa agagtagctc aaaatatgca	180
attaatttaa taatttctga tgatggtttt atctgcagta atatgtatat catctattag	240
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ctgattctta acattgtctt taatgaccac aagacaacca acag	344

&lt;210&gt; 342

&lt;211&gt; 592

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 342

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cctggcaggt aaaccaatgc caagagagtg atggaaacca ttggcaagac tttgttgatg	180
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tcctcagaa gagtgtaaag aaaagtcaga gatgctataa tagcagctat ttttaattggc	300
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tcagcatggg ctgtttgggtg caaatgcaaa agcacaggtc tttttagcat gctggctctc	420
cccggtgctc tatgcaaata atcgtcttct tctaaatttc tcttaggctt ctttttccaa	480
agttcttctt ggtttgtgat gtcttttctg ctttccatta attctataaa atagtatggc	540
ttcagccacc cactcttcgc cttagcttga ccgtgagtc cggctgccgc tg	592

&lt;210&gt; 343

&lt;211&gt; 382

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 343

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ggggtagttg gaagggactg aaattgtggg gggaaggtag gaggcacatc aataaagagg	360
aaaccaccaa gctgaaaaaa aa	382

&lt;210&gt; 344

&lt;211&gt; 536

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 344

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gtttaggggg atgccaagga taaggccagc tcagttatat gaagagaagc agaacaaca	180
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&lt;210&gt; 345

&lt;211&gt; 251



&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 345

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gcgtgggcca ggaaatcaca tcctacactg ccagagagcc agacacattt atggaacaga	180
aaataacata tcggatttgg agagacactg ccaactggct ggagattaat ccggacactg	240
gtgccatttc c	251

&lt;210&gt; 346

&lt;211&gt; 282

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(282)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 346

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ctaagtcttg ttaccaaaaa aaggaaaaag aaaagatctt ctcaagtaca aattctggga	120
agggagacta tacctggctc ttgccctaag tgagaggtct tccctccgc accaaaaaat	180
agaaaggctt tctatttcac tggcccaggt agggggaagg agagtaactt tgagtctgtg	240
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&lt;210&gt; 347

&lt;211&gt; 201

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(201)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 347

acacacataa tattataaaa tgccatctaa ttggaaggag ctttctatca ttgcaagtca	60
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tctgagactg actggaccca ccagaccca gggcaaagat acatgttacc atatcatctt	180
tataaagaat ttttttttgc c	201

&lt;210&gt; 348

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 348

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aggagacact ccagcatgg aggaggggtt atcttttcat cctaggtcag gtctacaatg	180
ggggaagggt ttattataga actcccaaca gccacactca ctctgccac ccaccgatg	240
gccctgcctc c	251

&lt;210&gt; 349

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 349

taaaaatcaa gccatttaaat tgtatctttg aaggtaaaca atatattgga gctggatcac	60
aacccttgag gatgccagag ctatgggtcc agaactgggt gtggtattat caacagagtt	120
cagaagggtc tgaactctac gtgttaccag agaacataat gcaattcatg cattccactt	180
agcaattttg taaaatacca gaaacagacc ccaagagtct ttcaagatga ggaaaattca	240
actctggtt t	251

&lt;210&gt; 350

&lt;211&gt; 908

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 350

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aatcgcag	908

&lt;210&gt; 351

&lt;211&gt; 472

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 351

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gatctgtcca caacaaactt gccctctcat gccttgctc tcaccatgct ctgctccagg	360
tcagccccc tttggcctgt ttgttttgtc aaaaacctaa tctgcttctt gcttttcttg	420
gtaatatata tttaggggaag atgttgcttt gccacacac gaagcaaagt aa	472

&lt;210&gt; 352

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 352

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caggctgcgt tccgtcctta cgatgaagac cagcatgcag ttccaaaca ttgccactac	180
atacatggaa aggaggggga agccaacca gaaatgggct ttctctaata ctgggatacc	240
aataagcaca a	251

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 <212> DNA  
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 gggctcctaa tgtagt 436

<210> 354  
 <211> 854  
 <212> DNA  
 <213> Homo sapien

<400> 354  
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 gactacatgc agtaatgggg tagatgtgtg tgggtgtgtc tcatctctgc aagggtgctt 480  
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 acacgggatg tcag 854

<210> 355  
 <211> 676  
 <212> DNA  
 <213> Homo sapien

<400> 355  
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 atccacaagt catacctgga tgtcagcgaa gagggcacgg aggcagcagc agccactggg 180  
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 gtgactttcc cacggccaaa aagctgttca cacctcacgc acctctgtgc ctgagtttgc 420  
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 attagatttt cttgacttgt atgtatctgt gagatcttga ataagtgacc tgacatctct 660  
 gcttaaagaa aaccag 676

<210> 356

<211> 574  
 <212> DNA  
 <213> Homo sapien

<400> 356

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aaaagtccac	aaaactgcag	tctttgctgg	gatagtaagc	caagcagtgc	ctggacagca	300
gagttctttt	cttgggcaac	agataaccag	acaggactct	aatcgtgctc	ttattcaaca	360
ttcttctgtc	tctgcctaga	ctggaataaa	aagccaatct	ctctcgtggc	acaggggaagg	420
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gatagacggc	acagggagct	cttaggtcag	cgtcgtggt	tggaggacat	tcctgagtc	540
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<210> 357  
 <211> 393  
 <212> DNA  
 <213> Homo sapien

<400> 357

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aagccacaac	caaracttga	ttttatcaac	aaaaaccctt	aaatataaac	ggsaaaaaag	180
atagatataa	ttattccagt	ttttttaaaa	cttaaaarat	attccattgc	cgaattaara	240
araarataag	tggtatatgg	aaagaagggc	attcaagcac	actaaaraaa	cctgaggkaa	300
gcataatctg	tacaaaatta	aactgtcctt	tttggcattt	taacaaattt	gcaacgktct	360
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<210> 358  
 <211> 630  
 <212> DNA  
 <213> Homo sapien

<400> 358

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gtagaacaat	ttgggcagag	ggaaccttat	agaccctaag	gtgggaaggt	tcaaagaact	300
gaaagagagc	tagaacagct	ggagccgttc	tccggtgtaa	agaggagtca	aagagataag	360
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gggtagactg	gactaggtaa	gactggaggc	aggtagacct	cttctaaggc	ctgcgatagt	540
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caagccagag	gttctctccac	aacaaccagt				630

<210> 359  
 <211> 620  
 <212> DNA  
 <213> Homo sapien

<400> 359

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ctcaccagaa	gaataaagtg	ctctgccagt	tattaaagga	ttactgctgg	tgaattaaat	180
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tgcaacatta tgcttcatga ataatatgta gaaagaaggt ctgatgaaaa tgacatcctt      420
aatgtaagat aactttataa gaattctggg tcaaataaaa ttctttgaag aaaacatcca      480
aatgtcattg acttatcaaa tactatcttg gcatataacc tatgaaggca aaactaaaca      540
aacaaaaagc tcacaccaa caaaaccatc aacttatttt gtattctata acatacgaga      600
ctgtaaagat gtgacagtgt

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620

&lt;210&gt; 360

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 360

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aaaaaaaaa agccagaaca acatgtgata gataatatga ttggctgcac acttcagac      60
tgatgaatga tgaacgtgat ggactattgt atggagcaca tcttcagcaa gagggggaaa      120
tactcatcat ttttggccag cagttgtttg atcaccaaac atcatgccag aatactcagc      180
aaaccttctt agctcttgag aagtcaaagt ccgggggaat ttattcctgg caattttaat      240
tggactcctt atgtgagagc agcggctacc cagctggggg ggtggagcga acccgtcact      300
agtggacatg cagtggcaga gctcctggta accacctaga ggaatacaca ggcacatgtg      360
tgatgccaag cgtgacacct gtagcactca aatttgtctt gtttttgtct ttcgggtgtg      420
agattcttag t

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431

&lt;210&gt; 361

&lt;211&gt; 351

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 361

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acactgattt ccgatcaaaa gaatcatcat ctttaccttg acttttcagg gaattactga      60
actttcttct cagaagatag ggcacagcca ttgccttggc ctcacttgaa gggctctgcat      120
ttgggtctctc tgggtctcttg ccaagtttcc cagccactcg agggagaaat atcggggaggt      180
ttgacttctt ccgggggcttt cccgagggct tcaccgtgag cctgcgggcc ctcaggggctg      240
caatcctgga ttcaatgtct gaaacctcgc tctctgcctg ctggacttct gaggccgtca      300
ctgccactct gtctccagc tctgacagct cctcatctgt ggtcctgttg t

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351

&lt;210&gt; 362

&lt;211&gt; 463

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 362

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acttcatcag gccataatgg gtgcctcccg tgagaatcca agcacctttg gactgcgcga      60
tgtagatgag ccggctgaag atcttgcgca tgcgcggctt cagggcgag ttcttgccgc      120
ccccggtcac agaaatgacc aggttgggtg ttttcagggt ccagtgtctg gtcagcagct      180
cgtaaaggat ttccgcgtcc gtgtcgcagg acagacgtat atacttccct ttcttcccca      240
gtgtctcaaa ctgaatatcc ccaaaggcgt cggtaggaaa ttccttggtg tgtttcttgt      300
agttccattt ctcaacttgg ttgatctggg tgccttccat gtgctggctc tgggcatagc      360
cacacttgca cacattctcc ctgataagca cgatggtgtg gacaggaagg aaggatttca      420
ttgagcctgc ttatggaaac tggattgtt agcttaata gac

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463

&lt;210&gt; 363

&lt;211&gt; 653

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (653)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 363

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acccccgagt ncctgnetgg catactgnga acgaccaacg acacacccaa gctcggcctc      60
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&lt;210&gt; 364

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 364

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aaaacaaggt gtagatgact agaattgtaa cattttaaga aaaccatagc atttgacaga      180
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&lt;210&gt; 365

&lt;211&gt; 356

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 365

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ccagtgtcat atttgggctt aaaatttcaa gaagggcact tcaaatggct ttgcatttgc      60
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taccagagca tcaagtctct gcagcaggtc attcttgggt aaagaaatga cttccacaaa      180
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gactgtcacg atgtgtatag tacagtttga caagcctggg tccatacaga ccgctggaga      300
acattcggca atgtcccctt ttagccagat ttcttcttcg agctcccga gagcag      356

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&lt;210&gt; 366

&lt;211&gt; 1851

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 366

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tcatacccat tgccagcagc ggcaccgtta gtcagggttt ctgggaatcc cacatgagta      60
cttcggtgtt cttcattctt cttcaatagc cataaatctt ctagctctgg ctggctgttt      120
tacttctctt taagcctttg tgactcttcc tetgatgtca gctttaagtc ttgttctgga      180
ttgctgtttt cagaagagat ttttaacatc tgtttttctt tgtagtcaga aagtaactgg      240
caaattacat gatgatgact agaaacagca tactctctgg ccgtctttcc agatcttgag      300
aagatacatc aacattttgc tcaagtagag ggctgactat acttgctgat ccacaacata      360
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tgattaaaaa tttcaccact tgctgttttt gctcatgtat accaagtagc agtgggtgtga      480
ggccatgctt gttttttgat tcgatatcag caccgtataa gagcagtgct ttggccatta      540

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&lt;210&gt; 367

&lt;211&gt; 668

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 367

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aaaaaaa						668

&lt;210&gt; 368

&lt;211&gt; 1512

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 368

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tgatctcgtg	cc					1512

&lt;210&gt; 369

&lt;211&gt; 1853

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 369

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&lt;210&gt; 370

&lt;211&gt; 2184

&lt;212&gt; DNA



&lt;213&gt; Homo sapien

&lt;400&gt; 370

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ggcacgagaa ttaaaaccct cagcaaaaca ggcatagaag ggacatacct taaagtaata      60
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&lt;210&gt; 371

&lt;211&gt; 1855

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1855)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 371

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&lt;210&gt; 372

&lt;211&gt; 1059

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 372

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&lt;210&gt; 373

&lt;211&gt; 1155

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 373

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&lt;210&gt; 374

&lt;211&gt; 2000

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 374

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 <212> DNA  
 <213> Homo sapien

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 <213> Homo sapien

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 Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser  
 35 40 45  
 Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg  
 50 55 60

Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val  
 65 70 75 80  
 Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val  
 85 90 95  
 Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr  
 100 105 110  
 His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp  
 115 120 125  
 Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp  
 130 135 140  
 Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser  
 145 150 155 160  
 Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys  
 165 170 175  
 Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala  
 180 185 190  
 Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly  
 195 200 205  
 Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr  
 210 215 220  
 Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr  
 225 230 235 240  
 Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu  
 245 250 255  
 Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys  
 260 265 270  
 Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu  
 275 280 285  
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 305 310 315 320  
 Ser Met Leu Phe Leu Val Ile Ile Met  
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&lt;210&gt; 377

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(148)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 377

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 35 40 45  
 Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu  
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 65 70 75 80  
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 85 90 95

Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro  
 100 105 110  
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp  
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 65 70 75 80  
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 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
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 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
 165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val

340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Asn Val Ser Arg Thr Arg Asn Lys  
 370 375 380  
 Pro Arg Thr His Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser  
 385 390 395 400  
 Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys  
 405 410 415  
 Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly  
 420 425 430  
 Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys  
 435 440 445  
 Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly  
 450 455 460  
 Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys  
 465 470 475 480  
 Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys  
 485 490 495  
 Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp  
 500 505 510  
 Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu  
 515 520 525  
 Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp  
 530 535 540  
 Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln  
 545 550 555 560  
 Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val  
 565 570 575  
 Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn  
 580 585 590  
 Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu  
 595 600 605  
 Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp  
 610 615 620  
 Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys  
 625 630 635 640  
 Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys  
 645 650 655  
 Asn Lys His Gly Leu Thr Pro Leu Leu Gly Val His Glu Gln Lys  
 660 665 670  
 Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala  
 675 680 685  
 Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly  
 690 695 700  
 Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser  
 705 710 715 720  
 Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser  
 725 730 735  
 His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln  
 740 745 750  
 Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys  
 755 760 765  
 Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser  
 770 775 780  
 Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp  
 785 790 795 800  
 Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly

805 810 815  
 Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn  
 820 825 830  
 Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe  
 835 840 845  
 Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser  
 850 855 860  
 Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn  
 865 870 875 880  
 Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu  
 885 890 895  
 Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile  
 900 905 910  
 Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn  
 915 920 925  
 Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro  
 930 935 940  
 Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu  
 945 950 955 960  
 Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe  
 965 970 975  
 Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His  
 980 985 990  
 Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser  
 995 1000 1005  
 Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu  
 1010 1015 1020  
 Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His  
 1025 1030 1035 1040  
 Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met  
 1045 1050 1055  
 Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met  
 1060 1065 1070  
 Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys  
 1075 1080 1085  
 Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr  
 1090 1095 1100  
 Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys  
 1105 1110 1115 1120  
 Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp  
 1125 1130 1135  
 Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His  
 1140 1145 1150  
 Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp  
 1155 1160 1165  
 Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg  
 1170 1175 1180  
 Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val  
 1185 1190 1195 1200  
 Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys  
 1205 1210 1215  
 Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly  
 1220 1225 1230  
 Asn Ser Glu Val Val Lys Leu Leu Asp Arg Arg Cys Gln Leu Asn  
 1235 1240 1245  
 Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys  
 1250 1255 1260  
 Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro



1265                      1270                      1275                      1280  
 Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr  
                                  1285                      1290                      1295  
 Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp  
                                  1300                      1305                      1310  
 Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Gly Val  
                                  1315                      1320                      1325  
 His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala  
                                  1330                      1335                      1340  
 Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala  
 1345                      1350                      1355                      1360  
 Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn  
                                  1365                      1370                      1375  
 Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr  
                                  1380                      1385                      1390  
 Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr  
                                  1395                      1400                      1405  
 Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu  
                                  1410                      1415                      1420  
 Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly  
 1425                      1430                      1435                      1440  
 Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn  
                                  1445                      1450                      1455  
 Lys Asp Gly Asp Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser  
                                  1460                      1465                      1470  
 Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly  
                                  1475                      1480                      1485  
 Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu  
                                  1490                      1495                      1500  
 Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys  
 1505                      1510                      1515                      1520  
 Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser  
                                  1525                      1530                      1535  
 Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu  
                                  1540                      1545                      1550  
 Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser  
                                  1555                      1560                      1565  
 Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe  
                                  1570                      1575                      1580  
 Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe  
 1585                      1590                      1595                      1600  
 Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly  
                                  1605                      1610                      1615  
 Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro  
                                  1620                      1625                      1630  
 Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln  
                                  1635                      1640                      1645  
 Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile  
                                  1650                      1655                      1660  
 Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser  
 1665                      1670                      1675                      1680  
 Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn  
                                  1685                      1690                      1695  
 Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr  
                                  1700                      1705                      1710  
 Met Lys His Gln Ser Gln Leu  
                                  1715

<210> 379  
 <211> 656  
 <212> PRT  
 <213> Homo sapien

<400> 379

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
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 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
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 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
 165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu  
 370 375 380  
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys  
 385 390 395 400  
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu  
 405 410 415

Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn  
 420 425 430  
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro  
 435 440 445  
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu  
 450 455 460  
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu  
 465 470 475 480  
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp  
 485 490 495  
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu  
 500 505 510  
 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys  
 515 520 525  
 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly  
 530 535 540  
 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser  
 545 550 555 560  
 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr  
 565 570 575  
 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln  
 580 585 590  
 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln  
 595 600 605  
 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys  
 610 615 620  
 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile  
 625 630 635 640  
 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu  
 645 650 655

&lt;210&gt; 380

&lt;211&gt; 671

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 380

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
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 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
 20 25 30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala

165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu  
 370 375 380  
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys  
 385 390 395 400  
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu  
 405 410 415  
 Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn  
 420 425 430  
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro  
 435 440 445  
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu  
 450 455 460  
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu  
 465 470 475 480  
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp  
 485 490 495  
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu  
 500 505 510  
 Asn Gly Gln Pro Glu Lys Arg Ser Gln Glu Pro Glu Ile Asn Lys Asp  
 515 520 525  
 Gly Asp Arg Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys Lys  
 530 535 540  
 His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly Ala  
 545 550 555 560  
 Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser Arg  
 565 570 575  
 Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr His  
 580 585 590  
 Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn  
 595 600 605  
 Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile  
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 Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys

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<210> 381
<211> 251
<212> DNA
<213> Homo sapien
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<400> 381

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ggtaacatgc	ttcccctaag	ggtatcccaa	cccaggggcc	tcaccatgac	ctctgagggg	120
ccaatatgcc	aggagaagca	ttggggagtt	gggggcaggt	gaaggaccca	ggactcacac	180
tccctggccc	tccaaggcag	aggagagggt	cctcaagaag	gtcaggagga	aaatccgtaa	240
caagcagtc	g					251

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<210> 382
<211> 3279
<212> DNA
<213> Homo sapiens
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<400> 382

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cactgggaag	ggacatcctg	cagaaggtag	gagtgaagaa	acacccgctg	caggggagggg	180
gagagccctg	cggcacctgg	gggagcagag	ggagcagcac	ctgcccaggc	ctgggaggag	240
gggcctggag	ggcgtgagga	ggagcagggg	ggctgcatgg	ctggagtgag	ggatcagggg	300
cagggcgcga	gatggcctca	cacagggaag	agagggcccc	tcttgcaggg	cctcacctgg	360
gccacaggag	gacatctgct	ttcctctgag	gagtccagg	ctgtggatgg	tgtggacag	420
aagaaggaca	gggcctggct	cagggtgtcca	gaggctgtcg	ctggcttccc	tttgggatca	480
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gtggctccag	gccttgcccc	tgcttggggc	ctacccagc	ctccctcaca	gtctctggc	600
cctcagtc	tccccctcac	tccatcctcc	atctggcctc	agtgggtcat	tctgatcact	660
gaactgacca	taccagccc	tgccccaggc	cctccatggc	tccccaatgc	cctggagagg	720
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gagccttggt	ccctctgttg	gactccctgc	ccatattctt	gtgggagtgg	gttctggaga	960
catttctgtc	tgttcctgag	agctgggaat	tgctctcagt	catctgcctg	cgcggttctg	1020
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tagggggaga	aactgaaagc	tgattaatta	caggaggttt	gttcaggttc	cccaaaccac	1860
cgtcagattt	gatgatttcc	tagcaggact	tacagaataa	aagagctatc	atgctgtggg	1920
ttattatggg	ttgttacatt	gataggatac	atactgaaat	cagcaacaaa	aacagatgta	1980
tagattagag	tgtggagaaa	acagaggaaa	acttgcagtt	acgaagactg	gcaacttggc	2040

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caaggatgta tgataatatg tacaaagtaa ttccaactga ggaagctcac ctgatacctta 2280
gtgtccaggg tttttactgg gggctctgtag gacgagtatg gagtacttga ataattgacc 2340
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ggcccaaggc cccaagtata tcaaggcact tgggcagaac atgccaagga atcaaatgct 2520
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gcagggctgc tgagtcaacc ttttattgta caggggatga gggaaaggga gaggatgagg 2640
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gttttcagac cttaaaaaaa aaaaaaaaaa aaaagtttt 3279

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&lt;210&gt; 383

&lt;211&gt; 154

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 383

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Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
      5                      10                      15

Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
      20                      25                      30

His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
      35                      40                      45

Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
      50                      55                      60

Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
      65                      70                      75                      80

Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
      85                      90                      95

Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
      100                     105                     110

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
      115                     120                     125

Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
      130                     135                     140

Ala Leu Glu Arg Gly His Leu Val Arg Glu
      145                     150

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<210> 384  
<211> 557  
<212> DNA  
<213> Homo sapiens

<400> 384  
ggatcctcta gagcgccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60  
aaagatgtgt tttgttttg actctctgtg gtcccttcca atgctgtggg tttccaacca 120  
ggggaagggg cctttttgca ttgccaagt ccataacccat gagcactact ctaccatggt 180  
tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240  
acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300  
ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360  
tccccagac acatcctaaa aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc 420  
ccttcttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480  
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttcc aaagtaaaaa 540  
aaaaaaaaa aaaaaaa 557

<210> 385  
<211> 337  
<212> DNA  
<213> Homo sapiens

<400> 385  
ttcccaggtg atgtgcgagg gaagacacat ttactatect tgatggggct gattccttta 60  
gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120  
tctcaaagcc atctgtgtgc ttcgagtacg gacacatcat cactcctgca ttgttgatca 180  
aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240  
tatcagacag gtccagtttc cgcaccaaca cctgctgggt ccctgtcgtg gtctggatct 300  
ctttggccac caattcccc tttccacat cccggca 337

<210> 386  
<211> 300  
<212> DNA  
<213> Homo sapiens

<400> 386  
gggcccgtca ccggcccagg cccgcctcgc cgagtcctcc tccccgggtg cctgcccga 60  
gcccgtcggg ccagaggggt gggcgcgagg gtgcctctac cggctggcgg ctgtaactca 120  
gcgaccttgg ccgaaggct ctagcaagga cccaccgacc ccagccgagg cggcgggcgc 180  
gcggactttg cccgggtgtg ggggcggagc ggactgcgtg tccgcggagc ggcagcgaag 240  
atgtagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300

<210> 387  
<211> 537  
<212> DNA  
<213> Homo sapiens

<400> 387  
gggcccagtc gggcaccaag ggactctttg caggcttccct tcctcggatc atcaaggctg 60  
ccccctcctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120  
tgaaccagga ccggcttctg ggcggctgaa aggggcaagg aggcaaggac cccgtctctc 180  
ccacggatgg ggagagggca ggaggagacc cagccaagt ccttttctc agcactgagg 240  
gagggggctt gtttcccttc cctcccggcg acaagctcca gggcagggt gtccctctgg 300  
gcgcccagc acttcctcag acacaacttc ttctgtctgc tccagtctg gggatcatca 360  
cttaccacc cccaagttc aagaccaaat cttccagctg ccccttctgt gtttccctgt 420  
gtttgtgta gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg ttagtctcc 480  
ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaaaa aaaaaaa 537

<210> 388  
<211> 520  
<212> DNA  
<213> Homo sapiens

<400> 388  
aggataattt ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60  
tgagggttaa ccagtttgca ttccccta atgtggaaaa taagaggact actcagcact 120  
gtttgaagat tgcctcttct acagcttctg agaattgtgt tatttcactt gccaaagtga 180  
ggacccccct cccaacatgc cccagcccac ccctaagcat ggccccttgt caccaggcaa 240  
ccaggaaact gctacttgtg gacctcacca gagaccagga gggtttggtt agctcacagg 300  
acttccccca cccagaaga ttagcatccc atactagact cataactcaac tcaactaggc 360  
tcatactcaa ttgatggta ttagacaatt ccatttcttt ctggttatta taaacagaaa 420  
atctttcttc ttctcattac cagtaaaggc tcttgggtatc tttctgttgg aatgatcttct 480  
atgaacttgt cttattttaa tgggtgggtt ttttctctgt 520

<210> 389  
<211> 365  
<212> DNA  
<213> Homo sapiens

<400> 389  
cggtgcccc gtttgacaga aggaaaggcg gagcttattc aaagtctaga gggagtggag 60  
gagttaaggc tggatttcag atctgcctgg ttccagccgc agtgtgccct ctgctcccc 120  
aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180  
aagcctatgg ccagctgtct ttgtgttccc tctcaccgc ctgtcctcac agctgagact 240  
cccaggaaac cttcagacta ctttctctg cttcagcaa ggggcgttgc ccacattctc 300  
tgagggtcag tggaagaacc tagactccca ttgctagagg tagaaagggg aagggtgctg 360  
gggag 365

<210> 390  
<211> 221  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(221)  
<223> n = A,T,C or G

<400> 390  
tgctctcca tcttggcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60  
tacacggnnt ctcattgggtg tggaacatct ctgcttgcgg ttccaggaag gcctctggct 120  
gctctangag tctgannga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180  
tcaaagtcta gaggagtggt aggagttaag gctggatttc a 221

<210> 391  
<211> 325  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(325)  
<223> n = A,T,C or G

<400> 391



tggagcaggt cccgaggcct cccatagagcc tggggccgac tctgtgncga tgcangcttt 60  
ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120  
tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180  
naanttngat ntccanagcc ctacccatcn tagttctgct ctcccaccgg ntaccagccc 240  
cactgcccag gaatcctaca gccagtaccc tgtcccgacg tctctaccta ccagtacgat 300  
gagacctccg gctactacta tgacc 325

<210> 392

<211> 277

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(277)

<223> n = A,T,C or G

<400> 392

atattgttta actccttctt ttatatcttt taacattttc atggngaaaag gttcacatct 60  
agtctcactt nggcnagnn ctctacttg agtctcttcc cgggcctggn ccagtnghaa 120  
antaccanga accgncatgn cttaanaacn ncctgggttn tgggttnntc aatgactgca 180  
tgacgtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggagg 240  
ctgaggatag agcgccgagt cctgtgttgc tggggaa 277

<210> 393

<211> 566

<212> DNA

<213> Homo sapiens

<400> 393

actagtccag tgtgggtggaa ttgcgggccc cgtcgacgga caggtcagct gtctggctca 60  
gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga ttaaattcag cctaaacgtt 120  
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180  
gagaaggctc agtttgtcca tcagcattat catgatata ggactgggta cttgggttaag 240  
gaggggtcta ggagatctgt cctttttaga gacaccttac ttataatgaa gtatttggga 300  
gggtgggttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacattttat 360  
catttattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420  
ttctgectca atgtttactg tgcctttgtt tttgctagtt tgtgttgttg aaaaaaaaaa 480  
cattctctgc ctgagtttta atttttgtcc aaagttattt taatctatac aattaaaagc 540  
ttttgcctat caaaaaaaaa aaaaaa 566

<210> 394

<211> 384

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(384)

<223> n = A,T,C or G

<400> 394

gaacatacat gtcccgccac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60  
tgcaaatng gaccgggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120  
gcaggaggac cgggctttta ggagttttta gctgagtgct actgtagacc ccaaatacca 180  
tccaagatt atcgggagaa agggggcagt aattacccaa atccgggttg agcatgacgt 240  
gaacatccag ttctctgata aggacgatgg gaaccagccc caggaccaa ttaccatcac 300  
agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360

tgagcagatg gtttctgagg acgt

384

<210> 395

<211> 399

<212> DNA

<213> Homo sapiens

<400> 395

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ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgc 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tatcagagggt ttcattcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagttctct ttggaaagcc tgggcatctc ctactacag acctctgacc atgggacggt 360
gcagcctgggt gagaccatcc aatcccaaat aaaatgcac 399
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<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 396

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tggagtnttc agtgcaaaca agccataaag cttcagtagc aaattactgt ctacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gttttagggga gggagtgagg gataaaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
atcaaagcag gtgctatcac tcaatgttag gccctgctct ttt 403
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<210> 397

<211> 100

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(100)

<223> n = A,T,C or G

<400> 397

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tccatccccg ctcttggttg gtnacagaat gactgacaaa 100
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<210> 398

<211> 278

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(278)

<223> n = A,T,C or G

<400> 398  
gcggccgcgt cgacagcagt tccgccagcg ctcccccctg ggtggggatg tgctgcacgc 60  
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120  
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggtgg actcatcatg 180  
ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240  
ctatggccgc ttcattangt ggctcaacaa ggagaagg 278

<210> 399  
<211> 298  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(298)  
<223> n = A,T,C or G

<400> 399  
acggaggtgg aggaagcgnc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60  
gggtgcccng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtgggct 120  
ccgagatcga gcgcatgggc ctggtcatgg accgcatggg ctccgtggag cgcgtgggct 180  
ccggcattga gcgcatgggc ccgctgggccc tcgaccacat ggctccanc attgancgca 240  
tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcatggg 298

<210> 400  
<211> 548  
<212> DNA  
<213> Homo sapiens

<400> 400  
acatcaacta cttcctcatt ttaaggatag gcagttccct tcateccett ttcctgcett 60  
gtacatgtac atgtatgaaa ttcccttctc ttaccgaact ctctccacac atcacaagg 120  
caaagaacca cacgcttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180  
tgagtctctt ttttccacgt ttaaggggcc atggcaggac ttagagttgc gagttaagac 240  
tgcagagggc tagagaatta ttccatacag gctttgaggc caccatgtc acttatcccg 300  
tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360  
gttggcccca taattctggg cctttgttgt ttgttttaac tacttgggca tcccaggaag 420  
ctttccagt atctctacc atgggcccc ctccctggat caagccctc ccaggccctg 480  
tccccagccc ctctgcccc agcccacccg cttgccttgg tgctcagccc tcccattggg 540  
agcaggtt 548

<210> 401  
<211> 355  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(355)  
<223> n = A,T,C or G

<400> 401  
actgtttcca tggtatgttt ctacacattg ctacctcagt gtccttgga acttagcttt 60  
tgatgtctcc aagtagtcca ctttcattta actctttgaa actgtatcat ctttgccaag 120  
taagagtggg ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180  
tataaatgaa tgtgctgaag caaagtgccc atggtggcgg cgaagaagan aaagatgtgt 240  
ttgtttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggt 300

cccttttgca ttgccaagtg ccataacccat gagcactact ctaccatggn tctgc 355

<210> 402

<211> 407

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(407)

<223> n = A,T,C or G

<400> 402

atgggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60  
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120  
aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180  
gaataaagat aaaaaagaga aggacattac aaaggtgggc ctgacctttg ataaatctca 240  
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300  
ttgtggagct tctccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360  
gntgatTTTTG ctgacaactc cttttctgaa gttttactca tttccaa 407

<210> 403

<211> 303

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(303)

<223> n = A,T,C or G

<400> 403

cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaattcc aggcacccaaa 60  
tcctaagcaa gagccatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120  
tagagaacaa gacctactca gtcattgaaca aaaaggcaga caccaacatg gatctcatgg 180  
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240  
tcttaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300  
gga 303

<210> 404

<211> 225

<212> DNA

<213> Homo sapiens

<400> 404

aagtgttaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60  
attgttaatg cactcattta cctttacatg gtgaaagtgc tctcttgatc ctacaaacag 120  
acattttcca ctctgttttc catagtgtgt aagtgtatca gatgtgttgg gcatgtgaat 180  
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcatt 225

<210> 405

<211> 334

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(334)

<223> n = A,T,C or G

<400> 405

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gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgagggttg tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
tcatccccat cccatgccaa aggaagacct tccctccttg gtcacagcc ttctctaggc 180
ttccagtgct cttcaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactctccac tctctcanng tggatcccac ccct 334
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<210> 406

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(216)

<223> n = A,T,C or G

<400> 406

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tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant 216
```

<210> 407

<211> 413

<212> DNA

<213> Homo sapiens

<400> 407

```
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcaccagtg tcagattcta cacctggcca ctgaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag 413
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<210> 408

<211> 183

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(183)

<223> n = A,T,C or G

<400> 408

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ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tncttaacta gttaatcctt aaagggctan ntaatcctta actagtcctt ccattgtgag 120
cattatcctt ccagtattcn ccttctnttt tatttactcc ttcctggcta cccatgtact 180
ntt 183
```

<210> 409

<211> 250

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(250)

<223> n = A,T,C or G

<400> 409

```
cccacgcatg ataagctctt tatctctgta agtcctgcta ggaaatcatc aaatctgacg 60
gtgggttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180
gcttcccagt gccccagga cagcgtgggc tatgtttaca gcgcntcctt gctggggggg 240
ggccttatgc                                     250
```

<210> 410

<211> 306

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(306)

<223> n = A,T,C or G

<400> 410

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ggctggttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtcttgcaa tccatttgc aggatccgtc tgtgcacatg cctctgtaga gagcagcatt 120
cccaggacc ttggaaacag ttggcactgt aagggtgctt ctccccaaga cacatcctaa 180
aagggtgtgt aatggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240
nactggttgg ctttttttgn atctttttta aactggaaag ttcaattgng aaaatgaata 300
tctnctgc                                     306
```

<210> 411

<211> 261

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(261)

<223> n = A,T,C or G

<400> 411

```
agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaagtgc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa gngaggcaa a                                     261
```

<210> 412

<211> 241

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(241)

<223> n = A,T,C or G

<400> 412

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gttcaatggt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
ctgggagatt tcaactggga cattgaattc ccaaactacc cangcaatta cccagccaac 240
a                                                                 241
```

<210> 413

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 413

```
aactcttaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctcc 60
ctcatccaag tttctagtag ctctcttttg ttgtgaagga taatcaaact gaacaacaaa 120
aagtttactc tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t          231
```

<210> 414

<211> 234

<212> DNA

<213> Homo sapiens

<400> 414

```
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggt ctctcttttg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaagctga ttcactatgg ggggagggtg attgaagtcc tcca      234
```

<210> 415

<211> 217

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(217)

<223> n = A,T,C or G

<400> 415

```
gcataggatt aagactgagt atcttttcta cattctttta acttttctaag gggcacttct 60
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cacttttcta 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc          217
```

<210> 416

<211> 213

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature  
 <222> (1)...(213)  
 <223> n = A,T,C or G

<400> 416  
 atgcataatnt aaagganact gcctcgcttt tagaagacat ctggncctgct ctctgcatga 60  
 ggacacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120  
 cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180  
 atattggaac agatggagtc tctactacaa aag 213

<210> 417  
 <211> 303  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(303)  
 <223> n = A,T,C or G

<400> 417  
 nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60  
 gtgggaaagg ctttactctg agttcaaadc ttcaagccca tcagagagtc cacactggag 120  
 agaagccata caaatgcaat gagggtggga agagcttcag gagggtattcc cattatcaag 180  
 ttcattctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240  
 tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300  
 agt 303

<210> 418  
 <211> 328  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(328)  
 <223> n = A,T,C or G

<400> 418  
 tttttggcgg tgggtggggca gggacgggac angagtctca ctctgttgcc caggctggag 60  
 tgcacaggca tgatctcggc tcactacaac cctcgctcc catgtccaag cgattcttgt 120  
 gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacacca gctagttttt 180  
 gtatttttag tagagacagg gtttcacat gttggccagg ctgggtctca actcctnacc 240  
 tcagnggtca ggctggtctc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300  
 aaagtgtctan gattacaggc cgtgagcc 328

<210> 419  
 <211> 389  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(389)  
 <223> n = A,T,C or G

<400> 419  
 cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgcatatg 60



```
acccttgagc catggactgg agcctgaaag gcagcgtaca ccctgctcct gatcttgctg 120
cttgtttccct ctctgtggct ccattcatag cacagttggt gcaactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggt gtgccaggca 240
ccggttctcc agccaccaac ctcaactcgt cccgcaaatg gcacatcagt tcttctaccc 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360
tggcagccac tcnggctgtg tcgacgcgg                                     389
```

&lt;210&gt; 420

&lt;211&gt; 408

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 420

```
gttcctccta actcctgcc aaaacagctc tctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gctttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtccattga cacttttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gactcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgcctatg acaaacctgg caagccccg                                     408
```

&lt;210&gt; 421

&lt;211&gt; 352

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(352)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 421

```
gctcaaaaat ctttttactg atnggcattg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggtct tttttgggtc cttcttctcc accacnata acttgagtc 180
ctccttcttg aagattcttt ggagattgtc tttgtcataa cccacagggt tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcattgc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttctc gg                                     352
```

&lt;210&gt; 422

&lt;211&gt; 337

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 422

```
atgccaccat gctggcaatg cagcggggcg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcgatagcaa ggtgccggcg atcggggcg cgtcaatcct ggccaaggte agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggtc 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccg attcaccgac 300
gcttcttccg ccggtacggc tggcctatga aaattat                                     337
```

&lt;210&gt; 423

&lt;211&gt; 310

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

<221> misc\_feature  
<222> (1)...(310)  
<223> n = A,T,C or G

<400> 423  
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60  
aggagaatga ggcctggcct gggagccctg tgcctactan aagcncatta gattatccat 120  
tcactgacag aacagggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtcc 180  
tccttcttga agattctttg gcagttgtct ttgtcataac ccacagggtg anaaacaagg 240  
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300  
tccgagtta 310

<210> 424  
<211> 370  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(370)  
<223> n = A,T,C or G

<400> 424  
gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60  
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120  
cactgacaga acagggtctt tttgggtcct tcttctccac cacgatatac ttgcagtcct 180  
ccttcttgaa gattcttttg cagttgtctt tgtcataacc cacagggtga gaaacatcct 240  
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300  
cacgaagggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360  
tccgtcgacg 370

<210> 425  
<211> 216  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(216)  
<223> n = A,T,C or G

<400> 425  
aattgctatn ntttattttg ccactcaaaa taattaccaa aaaaaaaaaa tnttaaata 60  
taacaacnca acatcaaggn aananaaca ggaatggntg actntgcata aatnggccga 120  
anattatcca ttatnttaag ggttgacttc aggnacagc acacagacaa acatgccag 180  
gaggntntca ggaccgctcg atgtntntg aggagg 216

<210> 426  
<211> 596  
<212> DNA  
<213> Homo sapiens

<400> 426  
cttccagtga ggataaccct gttgccccgg gccgagggtc tccattaggc tctgattgat 60  
tggcagtcag tgatggaagg gtgttctgat cattccgact gcccgaagg tgcctggcca 120  
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatgggtga 180  
gtgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240  
gacatcacgg caacttttaa tgaatgatt tgaagggcca ttaaggaggc cttcccgta 300

ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360  
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420  
gggtgatggc cttttcagct ttaacccaat ttgcactgcc ttggaagtgt agccaggaga 480  
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540  
gtcccgctgg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct 596

<210> 427

<211> 107

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(107)

<223> n = A,T,C or G

<400> 427

gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggnccag 60  
cccgggagca gccttanaga gtcctgttt gactgcccgg ctcagng 107

<210> 428

<211> 38

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(38)

<223> n = A,T,C or G

<400> 428

gaacttcena anaangactt tattcactat tttacatt 38

<210> 429

<211> 544

<212> DNA

<213> Homo sapiens

<400> 429

ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60  
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120  
atatccacga actcctgaag gactttctga tttatccaca atcaaatcat cggttttcag 180  
tttgatgggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240  
gccttcact tcagttacac ctcaactcacc atcctctcct gttggttctg tgetgettca 300  
agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360  
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420  
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480  
acctcaacaa gttagagaga tatgcatatc cagggatttt ttgccagggtg gtaggagaga 540  
ttat 544

<210> 430

<211> 507

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(507)

<223> n = A,T,C or G

<400> 430

```
cttatcncaa tggggctccc aaacttggt gtgcagtga aactccggg gaattttgaa 60
gaacactgac acccatcttc cccccgaca ctctgattta attgggctgc agtgagaaca 120
gagcatcaat ttaaaaagct gcccagaatg ttntcctggg cagcgttggt atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtga tggataaatc aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattctcttc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa 507
```

<210> 431

<211> 392

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(392)

<223> n = A,T,C or G

<400> 431

```
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtccctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggcttttac tctgctgttt ct 392
```

<210> 432

<211> 387

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(387)

<223> n = A,T,C or G

<400> 432

```
ggtatccta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtccaa gctctcgga gtccagccac tngaaacat gctcccttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tattttgctt ctgtctgnga 240
attctgttgc ttctggggca tttccttgng atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt 387
```

<210> 433

<211> 281

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

&lt;222&gt; (1) ... (281)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 433

```

ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgntattac accagnagg ntctctgtnt gccactggg 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281

```

&lt;210&gt; 434

&lt;211&gt; 484

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 434

```

ttttaaaata agcatttagt gctcagtcce tactgagtac tctttctctc cctcctctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tggtgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtaga tccatcttgc 180
ttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatgggtc tcagaacctt ttccccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480
ttaa 484

```

&lt;210&gt; 435

&lt;211&gt; 424

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 435

```

gcgcgcgtca gagcaggtea ctttctgcct tccacgtcct ccttcaagga agccccatgt 60
gggtagcttt caatatcgca ggttcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcgga ctggcgagag ttcagcgag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcattggtc ggggtgaccc 240
cttgagaga ggaaaaagc cacaagagg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaaacctc ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aac 424

```

&lt;210&gt; 436

&lt;211&gt; 667

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (667)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 436

```

accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcttgcccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataaggtg 120
agcctcttct ggaattcctc tgatttcaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacaggggt 300
gccaggtttg tcatagcact catcaaagtc cggccaacgt ctgtgcttcg aatataaacc 360

```

```

tggttcattgtt tataggactc attcaagaat tttctatatc tctttcttat atactctcca 420
agttcataat gctgctccat gccagctgg gtgagttggc caaatccttg tggccatgag 480
gattccttta tggggtcagt gggaaagggt tcaatgggac ttcggtctcc atgccgaaac 540
accaaagtca caaacttcaa ctccttggct agtacacttc ggtctagcca gaaaaaaagc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tggtgag                                     667

```

&lt;210&gt; 437

&lt;211&gt; 693

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 437

```

ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaaag ctggattggc aactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaaact tcagacagct ttttcagatc 180
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggtaactcct ctatttttcac cctcttggct tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatgtt tgtacagatc atggactatt ctctgtggac 360
catttctcca ggttaccta ggtgtcacta ttggggggac agccagcatc tttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tcctatttct aggcactgag ggctgtgggg taccttgttg tgccaaaaca gatcctgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc                                     693

```

&lt;210&gt; 438

&lt;211&gt; 360

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 438

```

ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac ctctgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgaggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcc aagaatcttc aagaaggagg 180
actgcaagta tatctggttg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

```

&lt;210&gt; 439

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(431)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 439

```

gttcctnnta actcctgcc aaaacagctc tctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gctttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaagggaat ctcattggcca caaggatttg 240
gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtccata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgctga cgcggccgcg 420
aatttagtag t                                     431

```

<210> 440  
<211> 523  
<212> DNA  
<213> Homo sapiens

<400> 440  
agagataaag cttagggtcaa agttcataga gttcccatga actatatgac tggccacaca 60  
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120  
tttaaagtgc tgaaatggaa cagattttcaa aaaaaaaccc cacaatctag ggtgggaaca 180  
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240  
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300  
actggaaaac tgctactatc tgtttttata ttctgttaa aatatatgag gctacagaac 360  
taaaaattaa aacctctttg tgtcccttgg tcctgggaaca tttatgttcc ttttaaagaa 420  
acaaaaatca aacttttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480  
tatatatatc atagcaaata agtcatctga tgagaacaag cta 523

<210> 441  
<211> 430  
<212> DNA  
<213> Homo sapiens

<400> 441  
gttcctccta actcctgcc aaaaacagctc tcctcaacat gagagctgca cccctcctcc 60  
tggccagggc agcaagcctt agccttggtt tcttgtttct gctttttttc tggctagacc 120  
gaagtgtact agccaaggag ttgaagtttg tgacttttgt gtttcggcat ggagaccgaa 180  
gtcccattga cacccttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240  
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300  
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360  
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgctga cgcggccgcg 420  
aatttagtag 430

<210> 442  
<211> 362  
<212> DNA  
<213> Homo sapiens

<400> 442  
ctaaggaatt agtagtggtc ccatcacttg tttggagtgt gctattctaa aagattttga 60  
tttcttgga tgacaattat attttaactt tgggtgggga aagagttata ggaccacagt 120  
cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attaagctat 180  
atgttttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240  
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattccttt 300  
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360  
tc 362

<210> 443  
<211> 624  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(624)  
<223> n = A,T,C or G

<400> 443  
tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60

```

ttgaaagaat taaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaacttgg ctctctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360
taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtac 420
atggtaaaca tccttattat taaagtcaac gctaaaaatga atgtgtgtgc atatgctaata 480
agtacagaga gagggcactt aaaccaacta agggcctgga gggaagggtt cctggaaaaga 540
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tattttaaact 600
ttgtccctat ctgctaaaca gatc                                     624

```

<210> 444

<211> 425

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(425)

<223> n = A,T,C or G

<400> 444

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gcacatcatt nntcttgcatt tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtgggtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcacctgt gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa tttagtagta 420
gtaga                                     425

```

<210> 445

<211> 414

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(414)

<223> n = A,T,C or G

<400> 445

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catgtttatg nttttggatt actttgggca cctagtgttt ctaaatcgtc tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattctt tgcattgtggc agattatttg atgtagtctt ctttaactag catataaatc 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaagtact aggtctctcc tcttgtattt tgaagcagt 360
tgggtgctgg attgataaaa aaaaaaaaaa tgcacgcggc cgcaatttta gtatg 414

```

<210> 446

<211> 631

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(631)



<223> n = A,T,C or G

<400> 446

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tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcagggtgtg 120
atgctgggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180
ccggtcctgt acgatttcag tatgtcttaa tgcgagctgt gattggaaca attcagattg 240
ctgtcatctg tgtgggtggc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaactttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgcttgg cattttgtgg 540
aatctacacc aatgaaaaca tgtactacag ctatatattga ttatgtatgg atatatattga 600
aatagtatac attgtcttga tgttttttct g 631
```

<210> 447

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

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cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcattgtt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attcctttat ggggtcagtg ggaaagggtg caatgggact tgggtctcca tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggtca gtacacttcg gtcta 585
```

<210> 448

<211> 93

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(93)

<223> n = A,T,C or G

<400> 448

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tgctcgtggg tcattctgan nnccgaactg accntgccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag 93
```

<210> 449

<211> 706

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(706)

<223> n = A,T,C or G

<400> 449

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ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggtcgggag cgtcccatc gccattcagg ctgcgcaact 240
gttgggaagg gcgatcggtg cgggcctctt cgtattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc caggggtttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcattgcacg 420
cgtacgtaag cttggatcct cttagcgggc cgctactac tactaaattc gcggccgcgt 480
cgacgtggga tccnactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggtgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcncccca 660
gcatggatga cagagtgaaa ctccatctta aaaaaaaaaa aaaaaa 706
```

<210> 450

<211> 493

<212> DNA

<213> Homo sapiens

<400> 450

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gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttaa aaggtaaaac aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcaactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcagggt agtgaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagtgag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggt cgacgcggcc 480
gcgaatttag tag 493
```

<210> 451

<211> 501

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 451

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gggcgcgtcc cattcgccat tcaggctgag caactgttgg gaagggcgat cgggtcgggc 60
ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattcgcgcc cgcgtcgacg tgggatccnc actgagagag 300
tggagagtga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacia 360
cgcncagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttgcaatga gctgagatca ggcenctgcn ccccgacatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501
```

<210> 452

<211> 51

<212> DNA

<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(51)  
<223> n = A,T,C or G

<400> 452  
agacggtttc accnttataa cnccttttag gatgggnntt ggggagcaag c 51

<210> 453  
<211> 317  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(317)  
<223> n = A,T,C or G

<400> 453  
tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60  
acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatgggtc tcagaaccat 120  
ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180  
taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240  
cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300  
taccatgtc tttatta 317

<210> 454  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 454  
ttcgaggtag aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60  
taagccacgc cacgctcttg aaggagtctt gaattctcct ctgctcactc agtagaacca 120  
agaagaccaa attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180  
ccttcttttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t 231

<210> 455  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 455  
taccaaagag ggcataataa tcagtctcac agtaggggtc accatcctcc aagtgaaaaa 60  
cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120  
gtttcaacgc attgatgact tctccaagga tcttcttttg gcatcgacca cattcagggg 180  
caaagaattt ctcatagcac agtcacaat acagggtccc tttctcctct a 231

<210> 456  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 456  
ttggcaggta cccttataaa gaagacacca taccttatgc gttattaggt ggaataatca 60  
ttccattcag tattatcggtt attattcttg gagaaacctt gtctgtttac tgtaaccttt 120  
tgcaactcaa ttcctttatc aggaataact acatagccac tatttataaa gccattggaa 180

cctttttatt tgggtgcagct gctagtcagt ccctgactga cattgccaaag t 231

<210> 457

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 457

cgaggtagcc aggggtctga aaatctctnn tttagtagtc gatagcaaaa ttgttcatca 60  
gcattcctta atatgatctt gctataatta gattttttctc cattagagtt catacagttt 120  
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180  
agttgtctaa atcgatgcct catttccctct gaggtgtcgc tggcctttgt g 231

<210> 458

<211> 231

<212> DNA

<213> Homo sapiens

<400> 458

aggtctgggt cccccactt ccactccct ctactctctc taggactggg ctgggccaaag 60  
agaagagggg tggttaggga agccgttgag acctgaagcc ccacctcta ccttccttca 120  
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180  
ggtcctgggt taggcatttt ggggggccag accccaggag aagaagattc t 231

<210> 459

<211> 231

<212> DNA

<213> Homo sapiens

<400> 459

ggtaccgagg ctgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60  
ccttcgcgaa acctgtggtg gccaccagt cctaacggga caggacagag agacagagca 120  
gccctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180  
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231

<210> 460

<211> 231

<212> DNA

<213> Homo sapiens

<400> 460

gcaggataaa catgtgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60  
cctatcaccc tattcttggg ggctgttct tcacagtgat catgaagcct agcagcaaat 120  
cccacctccc cacacgcaca cggccagcct ggagcccaca gaagggtcct cctgcagcca 180  
gtggagcttg gtccagcctc cagtccaccc ctaccaggct taaggataga a 231

<210> 461

<211> 231

<212> DNA

<213> Homo sapiens

<400> 461

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gcgtgtgctc cagaagagtg tgtgcatgcc agaggggaaa caggcgctg tgtgtcctgg 120  
gtgggggttca gtgaggagtg ggaaattggt tcagcagaac caagccgttg ggtgaataag 180  
aggggggatc catggcactg atagagccct atagtttcag agctgggaat t 231

<210> 462

<211> 231

<212> DNA

<213> Homo sapiens

<400> 462

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gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gcccaatctc atatgatgtg 120  
gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180  
tctagaggag gtatttaatt tcttctcact catccagtgt tgtatttagg a 231

<210> 463

<211> 231

<212> DNA

<213> Homo sapiens

<400> 463

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catttgacag gtgtcttttc ctctggacct cgggtgtccc atctgagtga gaaaaggcag 180  
tggggagggtg gatcttccag tcgaagcggc atagaagccc gtgtgaaaag c 231

<210> 464

<211> 231

<212> DNA

<213> Homo sapiens

<400> 464

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aaggacatca catatgaaga atgtttaagt tggaggtggc aacgtgaatt gcaaacaggg 120  
cctgcttcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180  
gggtgccagcg caccagctag atgctctgta acttctaggc cccattttcc c 231

<210> 465

<211> 231

<212> DNA

<213> Homo sapiens

<400> 465

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gtggcaaatt agcaacaaat tctgacatca tatttatggt ttctgtatct ttgttgatga 120  
aggatggcac aatttttgc tgtgttcata atatactcag attagtctag ctccatcaga 180  
taaactggag acatgcagga cattagggtg gtgttgttagc tctggtaatg a 231

<210> 466

<211> 231

<212> DNA

<213> Homo sapiens

<400> 466

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ggccttcgaa cagaacttgc cacataacca ggtataatag tttctaactt ttgcccagga 120  
cctgtgcgaat caaatattgt ggagaattcc ctagctggag aagtcacaaa gactataggc 180  
aataatggag accagtccca caagatgaca accagtcggt gtgtgcggct g 231

<210> 467  
 <211> 311  
 <212> DNA  
 <213> Homo sapiens

<400> 467  
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 tgtgccttaa cagaaggctct tgagattcta agtgggaatc atttcagtga ctgtcatgtg 180  
 gcatgggtct ctgcccaagc tcgtaatgag actatagcaa ggcggctgtg ggacgtcagt 240  
 tgtgacctgc tgggcctccc aatagactaa caggcagtgc cagttaggacc caagagaaga 300  
 ctgcagcaga c 311

<210> 468  
 <211> 3112  
 <212> DNA  
 <213> Homo sapiens

<400> 468  
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 tggaaggcac tggatgcctg atgatgaagt ggactttcaa actggggcac tactgaaacg 180  
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 catttgggtg aactgagaaa tggcataaca ccaaatttaa tatatgtcag atgttactat 540  
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 aaattgaaact gtttaacaaag gaatctcttg tcttgggtta tggctgagca cactgagca 660  
 tttccattcc agttggcttc ttgggtttgc tagctgcac actagtcac ttaaataaat 720  
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 atcatttcat atttctaacc ctcaaaacaa agctgttgta atatctgatc tctacgggtc 1920  
 cttctgggcc caacattctc catatatcca gccacactca tttttaatat ttagttccca 1980  
 gatctgtact gtgaccttct tacactgtag aataacatta ctcattttgt tcaaagaccc 2040  
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 gatctgtgaa caggctggga agcatctcaa gatctttcca gggttatact tactagcaca 2160  
 cagcatgatc attacggagt gaattatcta atcaacatca tctcagtggt ctttgcccat 2220  
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atatcacagg attaactttt ttttttaacc tggagaagaatt caatgtttaca tgcagctatg 2340
ggaattttaat tacatatattt gttttccagt gcaaagatga ctaagtcctt tatccctccc 2400
ctttgttttga ttttttttcc agtataaagt taaaatgctt agccttgtag tgaggctgta 2460
tacagccaca gcctctccccc atccctccag ccttatctgt catcaccatc aaccctccc 2520
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&lt;210&gt; 469

&lt;211&gt; 2229

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 469

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 470

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&lt;211&gt; 812

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 471

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<212> DNA

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<211> 5829

<212> DNA

<213> Homo sapiens

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&lt;211&gt; 1594

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 474

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1594

&lt;210&gt; 475

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<213> Homo sapiens

<220>  
<221> unsure  
<222> (33)  
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<212> DNA  
<213> Homo sapiens

<400> 476

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<210> 478
<211> 143
<212> PRT
<213> Homo sapiens
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Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
                20                      25                      30

Gly Glu Ile Thr Trp Thr His His His Thr Ile Thr Gly Thr Gln Thr
            35                      40                      45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
    50                      55                      60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
    65                      70                      75                      80

Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
            85                      90                      95

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His Gly His Thr Ser Thr Pro Ser His His His Thr His Cys Leu Trp  
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Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser  
 115 120 125

His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val  
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<210> 479

<211> 222

<212> PRT

<213> Homo sapiens

<400> 479

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln  
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Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr  
 20 25 30

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr  
 35 40 45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr  
 50 55 60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr  
 65 70 75 80

Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser  
 85 90 95

His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val  
 100 105 110

Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val  
 115 120 125

Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr  
 130 135 140

Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His  
 145 150 155 160

Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala  
 165 170 175

Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp  
 180 185 190

Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala  
 195 200 205

Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val  
 210 215 220

&lt;210&gt; 480

&lt;211&gt; 144

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 480

Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val  
                                   5                                  10                                  15

Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr  
                                   20                                  25                                  30

Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg  
                                   35                                  40                                  45

Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly  
                                   50                                  55                                  60

Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln  
                                   65                                  70                                  75                                  80

Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys  
                                   85                                  90                                  95

Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly  
                                   100                                  105                                  110

Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu  
                                   115                                  120                                  125

Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly  
                                   130                                  135                                  140

&lt;210&gt; 481

&lt;211&gt; 167

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 481

Met His Gly Pro Gln Val Leu Ala Arg Cys Ser Glu Cys Ala Cys Pro  
                                   5                                  10                                  15

Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg  
                                   20                                  25                                  30

Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser  
                                   35                                  40                                  45

Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys  
                                   50                                  55                                  60

Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro



65                                      70                                      75                                      80  
 Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser Ser Trp Arg  
    85                                      90                                      95  
 Ala Leu Ala Glu Val Thr Gly Cys Ser Leu Gly Pro Leu Gly Leu Ala  
    100                                      105                                      110  
 Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys Trp Ser His  
    115                                      120                                      125  
 Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr Ala Ala Phe  
    130                                      135                                      140  
 Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu Trp Ala Ser  
 145                                      150                                      155                                      160  
 Trp Leu Ser Arg Gly Arg Pro  
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<210> 482  
 <211> 143  
 <212> PRT  
 <213> Homo sapiens

<400> 482  
 Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val  
    5                                      10                                      15  
 Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu  
    20                                      25                                      30  
 Arg Ala Ser Trp Leu Pro Gly Gly Gly Pro Gln Ala Ile Leu Gly Arg  
    35                                      40                                      45  
 Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly  
    50                                      55                                      60  
 Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe  
    65                                      70                                      75                                      80  
 Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Thr  
    85                                      90                                      95  
 Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly  
    100                                      105                                      110  
 Ala Ser Gly Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys  
    115                                      120                                      125  
 Trp Met Ala Met Phe Pro Gln Pro Glu Trp Leu Pro Pro Asp Gly  
    130                                      135                                      140

<210> 483  
 <211> 143  
 <212> PRT

<213> Homo sapiens

<400> 483

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Met Glu Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
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Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala
      20              25              30
Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
      35              40              45
Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
      50              55              60
Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
      65              70              75              80
Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
      85              90              95
Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val
      100             105             110
Arg Leu Val Gln Ala Glu His Pro Pro Pro His Pro Leu Glu Glu Val
      115             120             125
Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys
      130             135             140

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<210> 484

<211> 30

<212> PRT

<213> Homo Sapien

<400> 484

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Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
  1      5              10              15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile
      20              25              30

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<210> 485

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 485

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31

<210> 486

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 486

gcgaattctc acgctgagta tttggcc

27

<210> 487

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 487

cccgaattct tagctgccca tccgaacgcc ttcac

36

<210> 488

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 488

gggaagcttc ttccccggct gcaccagctg tgc

33

<210> 489

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 489

Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala  
 1 5 10 15  
 Ser Val Ala

<210> 490

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 490

Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys  
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 Leu Ser His Ser  
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<210> 491

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 491

Thr	Cys	Leu	Ser	His	Ser	Val	Ala	Val	Val	Thr	Ala	Ser	Ala	Ala	Leu
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Thr	Gly	Phe	Thr												
				20											

<210> 492

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 492

Ala	Leu	Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr
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Leu	Ala	Ser	Leu												
				20											

<210> 493

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 493

Tyr	Thr	Leu	Ala	Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro
1				5					10					15	
Lys	Tyr	Arg	Gly												
				20											

<210> 494

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 494

Leu	Pro	Lys	Tyr	Arg	Gly	Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser
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Leu	Met	Ile	Ser												
				20											

<210> 495

<211> 20

<212> PRT

<213> Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 495

Asp Ser Leu Met Thr Ser Phe Leu Pro Gly Pro Lys Pro Gly Ala Pro  
1 5 10 15  
Phe Pro Asn Gly  
20

&lt;210&gt; 496

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 496

Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu  
1 5 10 15  
Pro Pro Pro Pro Ala  
20

&lt;210&gt; 497

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 497

Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val  
1 5 10 15  
Ser Val Arg Val  
20

&lt;210&gt; 498

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 498

Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val  
1 5 10 15  
Val Pro Gly Arg  
20

&lt;210&gt; 499

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

<223> Made in a lab

<400> 499

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 Ser Ala Phe Leu  
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<210> 500

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 500

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 Gly Ser Ile Val  
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<210> 501

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 501

Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met  
 1 5 10 15  
 Val Ser Ala Ala  
 20

<210> 502

<211> 414

<212> DNA

<213> Homo Sapien

<220>

<221> misc\_feature

<222> (1)...(414)

<223> n = A,T,C or G

<400> 502

caccatggag	acaggcctgc	gctggctttt	cctggtcgct	gtgctcaaag	gtgtccaatg	60
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ctgtagagtt	tttggaatng	acctcagtag	caatgcaatg	agctgggtcc	gccaggctcc	180
aggggaagggg	ctggaatgga	tggagccat	tgataattgt	ccacantacg	cgacctgggc	240
gaaaggccga	ttnatnattt	ccaaaacctn	gaccacgggtg	gatttgaaaa	tgaccagtcc	300
gacaaccgag	gacacggcca	cctatttttg	tggcagaatg	aatactggta	atagtggttg	360
gaagaatatt	tggggccccag	gcaccctggt	caccgtntcc	tcagggaac	ctaa	414

<210> 503

<211> 379

<212> DNA

<213> Homo Sapiens

<220>

<221> misc\_feature

<222> (1)...(379)

<223> n = A,T,C or G

<400> 503

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ctggtcacgc ctgggacacc cctgacactc acctgcaccg tntctggatt ngacatcagt	120
agctatggag tgagctgggt ccgccaggct ccaggaagg ggctgggata catcgatca	180
ttagtagtag tggtagattt tacgcgagct gggcgaaagg ccgattcacc atttccaaaa	240
cctngaccac ggtgatttg aaaatcacca gtttgacaac cgaggacacg gccacctatt	300
tntgtgccag aggggggttt aattataaag acatttgggg cccaggcacc ctggtcaccg	360
tntccttagg gcaacctaa	379

<210> 504

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 504

Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Glu	
1 5 10 15	
Asn Ser Ala	

<210> 505

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 505

Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn Asp Asn Val Thr	
1 5 10 15	
Asn Thr Ala Asn	
20	

<210> 506

<211> 407

<212> DNA

<213> Homo Sapien

<400> 506

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accgtctctg gattctccct cagtagcaat gcaatgatct gggcccgcca ggctccaggg	180
aaggggctgg aatacatcgg atacattagt tatgggtgta gcgcatacta cgcgagctgg	240
gtgaaaggcc gattcaccat ctccaaaacc tcgaccacgg tggatctgag aatgaccagt	300
ctgacaaccg aggacacggc cacctatttc tgtgccagaa atagtattt tagtggtatg	360
ttgtggggcc caggcaccct ggtcaccgtc tctcagggc aacctaa	407

<210> 507  
 <211> 422  
 <212> DNA  
 <213> Homo Sapien

<400> 507  
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 acagtctctg gattctccct cagcaactac gacctgaact gggtcgcca ggctccaggg 180  
 aaggggctgg aatggatcgg gatcattaat tatgttgga ggacggacta cgcgaactgg 240  
 gcaaaaggcc gggtcaccat ctccaaaacc tcgaccaccg tggatctcaa gatcgccagt 300  
 ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360  
 ggtccgtgct tgcgcctctg gggcccaggc accctgggtc ccgtctcctt agggcaacct 420  
 aa 422

<210> 508  
 <211> 411  
 <212> DNA  
 <213> Homo Sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(411)  
 <223> n = A,T,C or G

<400> 508  
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 cagtctctgg aatcgacctc agtagctact gcatgagctg ggtccgccag gctccaggga 180  
 aggggctgga atggatcgga atcattgga ctctgggtga cacatactac gcgagggtgg 240  
 cgaaaggccg attcaccatc tccaaaacct cgaccacggt gcatntgaaa atcnccagtc 300  
 cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360  
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<210> 509  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 509  
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 1 5 10 15

<210> 510  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 510  
 Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile  
 1 5 10 15



<210> 511  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys  
 1 5 10 15

<210> 512  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 512

Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu  
 1 5 10 15

<210> 513  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 513

Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu  
 1 5 10 15

<210> 514  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 514

Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 1 5 10 15

<210> 515  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

&lt;400&gt; 515

Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg  
1 5 10 15

&lt;210&gt; 516

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 516

Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln  
1 5 10 15

&lt;210&gt; 517

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 517

Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met  
1 5 10 15

&lt;210&gt; 518

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 518

Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly  
1 5 10 15

&lt;210&gt; 519

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 519

Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys  
1 5 10 15  
Gly

&lt;210&gt; 520

&lt;211&gt; 25

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 520

Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr  
 1 5 10 15  
 Glu Ala Arg Arg His Tyr Asp Glu Gly  
 20 25

&lt;210&gt; 521

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 521

Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu  
 1 5 10 15  
 Pro Pro Pro Pro Ala  
 20

&lt;210&gt; 522

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 522

Leu Leu Val Val Pro Ala Ile Lys Lys Asp Tyr Gly Ser Gln Glu Asp  
 1 5 10 15  
 Phe Thr Gln Val  
 20

&lt;210&gt; 523

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(254)

&lt;223&gt; Xaa = any amino acid

&lt;400&gt; 523

Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile  
 1 5 10 15  
 Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile  
 20 25 30  
 Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu  
 35 40 45

Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln  
 50 55 60  
 Trp Val Leu Ser Ala Thr His Cys Phe Gln Asn Ser Tyr Thr Ile Gly  
 65 70 75 80  
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met  
 85 90 95  
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu  
 100 105 110  
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu  
 115 120 125  
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala  
 130 135 140  
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg  
 145 150 155 160  
 Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu  
 165 170 175  
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys  
 180 185 190  
 Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly  
 195 200 205  
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly  
 210 215 220  
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu  
 225 230 235 240  
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 245 250

&lt;210&gt; 524

&lt;211&gt; 765

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 524

atggccacag	caggaaatcc	ctggggctgg	ttctgggggt	acctcattcct	tggtgtcgca	160
ggatcgctcg	tctctggtag	ctgcagccaa	atcataaacg	gcgaggactg	cagcccgcac	120
tcgcagccct	ggcaggcggc	actggtcatg	gaaaacgaat	tggtctgctc	ggcgctcctg	180
gtgcatccgc	agtgggtgct	gtcagccgca	cactgtttcc	agaactccta	caccatcggg	240
ctgggcctgc	acagtcttga	ggccgaccaa	gagccaggga	gccagatggt	ggaggccagc	300
ctctccgtac	ggcacccaga	gtacaacaga	cccttgctcg	ctaacgacct	catgctcatc	360
aagttggacg	aatccgtgtc	cgagtctgac	accatccgga	gcacagcat	tgcttcgcag	420
tgccctaccg	cggggaactc	ttgcctcggt	tctggctggg	gtctgctggc	gaacggcaga	480
atgcctaccg	tgctgcagtg	cgtgaacgtg	tcggtgggtg	ctgaggaggt	ctgcagtaag	540
ctctatgacc	cgctgtacca	ccccagcatg	ttctgcgccg	gcggagggca	agaccagaag	600
gactcctgca	acggtgactc	tggggggccc	ctgatctgca	acgggtactt	gcagggcctt	660
gtgtctttcg	gaaaagcccc	gtgtggccaa	gttggcgtgc	caggtgtcta	caccaacctc	720
tgcaaattca	ctgagtggat	agagaaaacc	gtccaggcca	gttaa		765

&lt;210&gt; 525

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 525

Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile  
 1 5 10 15  
 Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile  
 20 25 30  
 Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu

35 40 45  
 Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln  
 50 55 60  
 Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly  
 65 70 75 80  
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met  
 85 90 95  
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu  
 100 105 110  
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu  
 115 120 125  
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala  
 130 135 140  
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg  
 145 150 155 160  
 Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu  
 165 170 175  
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys  
 180 185 190  
 Ala Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly  
 195 200 205  
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly  
 210 215 220  
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu  
 225 230 235 240  
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 245 250

&lt;210&gt; 526

&lt;211&gt; 963

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 526

atgagttcct gcaacttcac acatgccacc tttgtgctta ttggtatccc aggattagag 60  
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 aactgcatcg tgggtcttcat cgtaaggacg gaacgcagcc tgcacgctcc gatgtacctc 180  
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 cgttatgtgg ccatctgcca cccactgcgc catgctgcag tgctcaacaa tacagtaaca 420  
 gccagattg gcatcgtggc tgtggtccgc ggatccctct tttttttccc actgcctctg 480  
 ctgatcaagc ggctggcctt ctgccactcc aatgtcctct cgcactccta ttgtgtccac 540  
 caggatgtaa tgaagtggc ctatgcagac actttgcca atgtggtata tggctttact 600  
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 caccgctttg gaaacagcct tcatccatt gtgcgtgttg tcatgggtga catctacctg 840  
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 cgggtgctgg ctatgttcaa gatcagctgt gacaaggact tgcaggctgt gggaggcaag 960  
 tga 963

&lt;210&gt; 527

&lt;211&gt; 320

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 527

Met Ser Ser Cys Asn Phe Thr His Ala Thr Phe Val Leu Ile Gly Ile  
                                   5                                  10                                  15  
 Pro Gly Leu Glu Lys Ala His Phe Trp Val Gly Phe Pro Leu Leu Ser  
                                   20                                  25                                  30  
 Met Tyr Val Val Ala Met Phe Gly Asn Cys Ile Val Val Phe Ile Val  
                                   35                                  40                                  45  
 Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met  
                                   50                                  55                                  60  
 Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile  
                                   65                                  70                                  75                                  80  
 Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Phe Glu Ala Cys  
                                   85                                  90                                  95  
 Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr  
                                   100                                  105                                  110  
 Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro  
                                   115                                  120                                  125  
 Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly  
                                   130                                  135                                  140  
 Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu  
                                   145                                  150                                  155                                  160  
 Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser  
                                   165                                  170                                  175  
 Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu  
                                   180                                  185                                  190  
 Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val  
                                   195                                  200                                  205  
 Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val  
                                   210                                  215                                  220  
 Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys  
                                   225                                  230                                  235                                  240  
 Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly  
                                   245                                  250                                  255  
 Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg  
                                   260                                  265                                  270  
 Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro  
                                   275                                  280                                  285  
 Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala  
                                   290                                  295                                  300  
 Met Phe Lys Ile Ser Cys Asp Lys Asp Leu Gln Ala Val Gly Gly Lys

305

310

315

320

<210> 528  
<211> 20  
<212> DNA  
<213> Homo Sapien

<400> 528  
actatgggtcc agaggctgtg

20

<210> 529  
<211> 20  
<212> DNA  
<213> Homo Sapien

<400> 529  
atcacctatg tgccgcctct

20

<210> 530  
<211> 1852  
<212> DNA  
<213> Homo sapiens

&lt;400&gt; 530

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tttctcttga gaactgcaac aataaataca aggatgctgg attttgtcaa atgccttttc 180  
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ggagtctctc cttcatagt tcatccatag gctccagagg aaaattatat tattttgtta 480  
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gcgaatttaa atgcgctgga tagatatgga agaactgctc tcatacttgc tgtatgttgt 1500  
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tttctgacta caaagaaaaa cagatgttaa aaatctcttc tgaaaacagc aatccagaac 1680  
aagacttaaa gctgacatca gaggaagagt cacaaggct taaaggaagt gaaaacagcc 1740  
agccagagct agaagattta tggctattga agaagaatga agaacacgga agtactcatg 1800  
tgggattccc agaaaacctg actaacgggt cgcgtgctgg caatgggtgat ga 1852

<210> 531  
<211> 879

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 531

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gtcatgctca gggacacgga tgtgaacaag agggacaagc aaaagaggac tgctctacat 360
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cttaatgtcc ttgacaacaa aaagaggaca gctctgacaa aggccgtaca atgccaggaa 480
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&lt;210&gt; 532

&lt;211&gt; 292

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 532

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Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp
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Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu
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Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser
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Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu
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Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu
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Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile
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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;223&gt; n=A,T,C or G

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cgtctatcag gttttgtgcc ttaagagact acagnagtca gaagctcatt ttaaaggag 4560
taggacagag ttgtcacagg tttttgttgg tgtttktatt gccccaaaaa ttacatgcta 4620
atttccattt atactagggt attctattta cttgaagact gtgaagtgtc cattttgtct 4680
cattgttttc tttgacatam ctaggatcca ttatttcccc tgaaggcttc ttgkagaaaa 4740
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gagtgtgtac cccttactcc ccatcaaaaa aaaaaatgga tacatgggta aaggatagaa 4860
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tttgtccttc gtatagcaag ttttttgtc atcagcagag agcaacagat gttttattga 5640
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agctgttcaa ctctagtac ttagaatac acgtatgggt aatgttcagt ccaacaaacc 5760
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tggaactttt agggttaaaga cagtcataata aacgtcctgt ttctgtttta atgttatcat 5940
agaatttttt aatgaaacta aattcaattg aaataaatga tagttttcat ctccaaaaaa 6000
aaaaaaaaag ggcggcccg ctagtctag agggcccggt ttaaaccgc tgatcagcct 6060
cgactgtgcc ttctagtgtc cagccatctg ttgtttggcc ctccccctg ccttcttga 6120
ccctggaagg ggccactccc

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&lt;210&gt; 537

&lt;211&gt; 1228

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 537

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Met Leu Pro Val Tyr Gln Glu Val Lys Pro Asn Pro Leu Gln Asp Ala
          5                      10                      15

```

```

Asn Leu Cys Ser Arg Val Phe Phe Trp Trp Leu Asn Pro Leu Phe Lys
          20                      25                      30

```

```

Ile Gly His Lys Arg Arg Leu Glu Glu Asp Asp Met Tyr Ser Val Leu
          35                      40                      45

```

```

Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu Leu Gln Gly Phe Trp
          50                      55                      60

```

```

Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala Gln Lys Pro Ser Leu

```

65	70	75	80
Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser Tyr Leu Val Leu Gly	85	90	95
Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val Ile Gln Pro Ile Phe	100	105	110
Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr Asp Pro Met Asp Ser	115	120	125
Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr Val Leu Thr Phe Cys	130	135	140
Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr Phe Tyr His Val Gln	145	150	155
Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys His Met Ile Tyr Arg	165	170	175
Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly Lys Thr Thr Thr Gly	180	185	190
Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn Lys Phe Asp Gln Val	195	200	205
Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro Leu Gln Ala Ile Ala	210	215	220
Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile Ser Cys Leu Ala Gly	225	230	235
Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln Ser Cys Phe Gly Lys	245	250	255
Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr Phe Thr Asp Ala Arg	260	265	270
Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile Arg Ile Ile Lys Met	275	280	285
Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile Thr Asn Leu Arg Lys	290	295	300
Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys Leu Arg Gly Met Asn	305	310	315
Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile Val Phe Val Thr Phe	325	330	335
Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr Ala Ser Arg Val Phe	340	345	350
Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu Thr Val Thr Leu Phe	355	360	365
Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg	370	375	380

Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg  
 385 390 395 400  
 Gln Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr  
 405 410 415  
 Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser  
 420 425 430  
 Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly  
 435 440 445  
 Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro  
 450 455 460  
 Ser His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln  
 465 470 475 480  
 Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly  
 485 490 495  
 Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala  
 500 505 510  
 Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile  
 515 520 525  
 Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn  
 530 535 540  
 Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp  
 545 550 555 560  
 Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu  
 565 570 575  
 Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His  
 580 585 590  
 Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp  
 595 600 605  
 Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly  
 610 615 620  
 Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln  
 625 630 635 640  
 Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu  
 645 650 655  
 Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly  
 660 665 670  
 Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu  
 675 680 685



Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr  
 690 695 700  
 Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Leu  
 705 710 715 720  
 Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln Asp Trp Trp Leu Ser  
 725 730 735  
 Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val Thr Val Asn Gly Gly  
 740 745 750  
 Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp Tyr Leu Gly Ile Tyr  
 755 760 765  
 Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly Ile Ala Arg Ser Leu  
 770 775 780  
 Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln Thr Leu His Asn Lys  
 785 790 795 800  
 Met Phe Glu Ser Ile Leu Lys Ala Pro Val Leu Phe Phe Asp Arg Asn  
 805 810 815  
 Pro Ile Gly Arg Ile Leu Asn Arg Phe Ser Lys Asp Ile Gly His Leu  
 820 825 830  
 Asp Asp Leu Leu Pro Leu Thr Phe Leu Asp Phe Ile Gln Thr Leu Leu  
 835 840 845  
 Gln Val Val Gly Val Val Ser Val Ala Val Ala Val Ile Pro Trp Ile  
 850 855 860  
 Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe Ile Phe Leu Arg Arg  
 865 870 875 880  
 Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg Leu Glu Ser Thr Thr  
 885 890 895  
 Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser Leu Gln Gly Leu Trp  
 900 905 910  
 Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys Gln Glu Leu Phe Asp  
 915 920 925  
 Ala His Gln Asp Leu His Ser Glu Ala Trp Phe Leu Phe Leu Thr Thr  
 930 935 940  
 Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile Cys Ala Met Phe Val  
 945 950 955 960  
 Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala Lys Thr Leu Asp Ala  
 965 970 975  
 Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu Thr Leu Met Gly Met  
 980 985 990  
 Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val Glu Asn Met Met Ile



Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val  
 50 55 60  
 Ile Gln Pro Ile Phe Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr  
 65 70 75 80  
 Asp Pro Met Asp Ser Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr  
 85 90 95  
 Val Leu Thr Phe Cys Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr  
 100 105 110  
 Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys  
 115 120 125  
 His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly  
 130 135 140  
 Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn  
 145 150 155 160  
 Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro  
 165 170 175  
 Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile  
 180 185 190  
 Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln  
 195 200 205  
 Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr  
 210 215 220  
 Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile  
 225 230 235 240  
 Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile  
 245 250 255  
 Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys  
 260 265 270  
 Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile  
 275 280 285  
 Val Phe Val Thr Phe Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr  
 290 295 300  
 Ala Ser Arg Val Phe Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu  
 305 310 315 320  
 Thr Val Thr Leu Phe Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala  
 325 330 335  
 Ile Val Ser Ile Arg Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile  
 340 345 350

Ser Gln Arg Asn Arg Gln Leu Pro Ser Asp Gly Lys Lys Met Val His  
 355 360 365  
 Val Gln Asp Phe Thr Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr  
 370 375 380  
 Leu Gln Gly Leu Ser Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val  
 385 390 395 400  
 Val Gly Pro Val Gly Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu  
 405 410 415  
 Gly Glu Leu Ala Pro Ser His Gly Leu Val Ser Val His Gly Arg Ile  
 420 425 430  
 Ala Tyr Val Ser Gln Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser  
 435 440 445  
 Asn Ile Leu Phe Gly Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val  
 450 455 460  
 Ile Lys Ala Cys Ala Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly  
 465 470 475 480  
 Asp Leu Thr Val Ile Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln  
 485 490 495  
 Lys Ala Arg Val Asn Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile  
 500 505 510  
 Tyr Leu Leu Asp Asp Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg  
 515 520 525  
 His Leu Phe Glu Leu Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr  
 530 535 540  
 Ile Leu Val Thr His Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile  
 545 550 555 560  
 Leu Ile Leu Lys Asp Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu  
 565 570 575  
 Phe Leu Lys Ser Gly Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn  
 580 585 590  
 Glu Glu Ser Glu Gln Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn  
 595 600 605  
 Arg Thr Phe Ser Glu Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro  
 610 615 620  
 Ser Leu Lys Asp Gly Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro  
 625 630 635 640  
 Val Thr Leu Ser Glu Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln  
 645 650 655  
 Ala Tyr Lys Asn Tyr Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile

660					665					670					
Phe	Leu	Ile	Leu	Leu	Asn	Thr	Ala	Ala	Gln	Val	Ala	Tyr	Val	Leu	Gln
	675						680					685			
Asp	Trp	Trp	Leu	Ser	Tyr	Trp	Ala	Asn	Lys	Gln	Ser	Met	Leu	Asn	Val
	690						695					700			
Thr	Val	Asn	Gly	Gly	Gly	Asn	Val	Thr	Glu	Lys	Leu	Asp	Leu	Asn	Trp
	705					710					715				720
Tyr	Leu	Gly	Ile	Tyr	Ser	Gly	Leu	Thr	Val	Ala	Thr	Val	Leu	Phe	Gly
				725					730					735	
Ile	Ala	Arg	Ser	Leu	Leu	Val	Phe	Tyr	Val	Leu	Val	Asn	Ser	Ser	Gln
			740					745					750		
Thr	Leu	His	Asn	Lys	Met	Phe	Glu	Ser	Ile	Leu	Lys	Ala	Pro	Val	Leu
		755					760					765			
Phe	Phe	Asp	Arg	Asn	Pro	Ile	Gly	Arg	Ile	Leu	Asn	Arg	Phe	Ser	Lys
	770					775					780				
Asp	Ile	Gly	His	Leu	Asp	Asp	Leu	Leu	Pro	Leu	Thr	Phe	Leu	Asp	Phe
	785					790					795				800
Ile	Gln	Thr	Leu	Leu	Gln	Val	Val	Gly	Val	Val	Ser	Val	Ala	Val	Ala
			805					810						815	
Val	Ile	Pro	Trp	Ile	Ala	Ile	Pro	Leu	Val	Pro	Leu	Gly	Ile	Ile	Phe
			820					825					830		
Ile	Phe	Leu	Arg	Arg	Tyr	Phe	Leu	Glu	Thr	Ser	Arg	Asp	Val	Lys	Arg
		835					840					845			
Leu	Glu	Ser	Thr	Thr	Arg	Ser	Pro	Val	Phe	Ser	His	Leu	Ser	Ser	Ser
	850					855					860				
Leu	Gln	Gly	Leu	Trp	Thr	Ile	Arg	Ala	Tyr	Lys	Ala	Glu	Glu	Arg	Cys
	865					870					875				880
Gln	Glu	Leu	Phe	Asp	Ala	His	Gln	Asp	Leu	His	Ser	Glu	Ala	Trp	Phe
			885					890						895	
Leu	Phe	Leu	Thr	Thr	Ser	Arg	Trp	Phe	Ala	Val	Arg	Leu	Asp	Ala	Ile
			900					905					910		
Cys	Ala	Met	Phe	Val	Ile	Ile	Val	Ala	Phe	Gly	Ser	Leu	Ile	Leu	Ala
		915					920					925			
Lys	Thr	Leu	Asp	Ala	Gly	Gln	Val	Gly	Leu	Ala	Leu	Ser	Tyr	Ala	Leu
	930					935					940				
Thr	Leu	Met	Gly	Met	Phe	Gln	Trp	Cys	Val	Arg	Gln	Ser	Ala	Glu	Val
	945					950					955				960
Glu	Asn	Met	Met	Ile	Ser	Val	Glu	Arg	Val	Ile	Glu	Tyr	Thr	Asp	Leu
			965					970						975	

Glu Lys Glu Ala Pro Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp  
                   980                                  985                                  990  
 Pro His Glu Gly Val Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser  
                   995                                  1000                                  1005  
 Pro Gly Gly Pro Leu Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser  
                   1010                                  1015                                  1020  
 Gln Glu Lys Val Gly Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser  
                   1025                                  1030                                  1035                                  1040  
 Leu Ile Ser Ala Leu Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp  
                                   1045                                  1050                                  1055  
 Ile Asp Lys Ile Leu Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys  
                                   1060                                  1065                                  1070  
 Lys Met Ser Ile Ile Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met  
                   1075                                  1080                                  1085  
 Arg Lys Asn Leu Asp Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp  
                   1090                                  1095                                  1100  
 Asn Ala Leu Gln Glu Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro  
                   1105                                  1110                                  1115                                  1120  
 Gly Lys Met Asp Thr Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val  
                                   1125                                  1130                                  1135  
 Gly Gln Arg Gln Leu Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn  
                                   1140                                  1145                                  1150  
 Gln Ile Leu Ile Ile Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr  
                   1155                                  1160                                  1165  
 Asp Glu Leu Ile Gln Lys Lys Ile Arg Glu Lys Phe Ala His Cys Thr  
                   1170                                  1175                                  1180  
 Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys  
                   1185                                  1190                                  1195                                  1200  
 Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr  
                                   1205                                  1210                                  1215  
 Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln  
                   1220                                  1225                                  1230  
 Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg  
                   1235                                  1240                                  1245  
 Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser  
                   1250                                  1255                                  1260

&lt;210&gt; 539

&lt;211&gt; 10

&lt;212&gt; PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 539

Cys Leu Ser His Ser Val Ala Val Val Thr  
1 5 10

<210> 540

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 540

Ala Val Val Thr Ala Ser Ala Ala Leu  
1 5

<210> 541

<211> 14

<212> PRT

<213> Homo sapiens

<400> 541

Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu  
5 10

<210> 542

<211> 15

<212> PRT

<213> Homo sapiens

<400> 542

Thr Gln Val Val Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
5 10 15

<210> 543

<211> 12

<212> PRT

<213> Homo sapiens

<400> 543

Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val  
5 10

<210> 544

<211> 18

<212> PRT

<213> Homo sapiens

<400> 544

Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe

5

10

15

Met Thr

&lt;210&gt; 545

&lt;211&gt; 18

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 545

Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala  
                           5                          10                          15

Ser Val

&lt;210&gt; 546

&lt;211&gt; 29

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 546

Phe Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly  
                           5                          10                          15

Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met  
                           20                          25

&lt;210&gt; 547

&lt;211&gt; 58

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 547

Val Ala Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu  
                           5                          10                          15

Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu  
                           20                          25                          30

Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys  
                           35                          40                          45

Cys Arg Met Pro Arg Thr Leu Arg Arg Leu  
                           50                          55

&lt;210&gt; 548

&lt;211&gt; 18

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 548

Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu



200

5

10

15

Glu Cys

&lt;210&gt; 549

&lt;211&gt; 18

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 549

Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg  
5 10 15

Gln Ala

&lt;210&gt; 550

&lt;211&gt; 14

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 550

Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe  
5 10

&lt;210&gt; 551

&lt;211&gt; 11

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 551

Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
1 5 10